ABSTRACT:
Nucleotides of nucleosides or ▼ bases ▼ having known cytotoxic activity are reacted with steroids, preferably corticosteroids, to form corresponding cytotoxic ▼ nucleoside ▼ -corticosteroid phosphodiester ▼ analogues ▼ of the formula: ##STR1## wherein: steroid is the residue formed by removal of a hydroxyl hydrogen atom from a natural or synthetic adrenal corticosteroid containing the characteristic cyclopentanophenanthrene nucleus which is esterified to the phosphate moiety at the 21-position;
sugar is a naturally occurring pentose or deoxypentose in the furanose form, preferably ribose, deoxyribose, lyxose, xylose or arabinose and especially ribose, deoxyribose or arabinose, which is esterified to the phosphate moiety at the 5'-position and ▼ covalently ▼ bonded to the heterocycle moiety at the 1'-position to form a nucleoside; and heterocycle is a purine, pyrimidine, hydrogenated pyrimidine, triazolopurine or similar nucleoside ▼ base ▼ .
The conjugates exhibit an enhanced therapeutic index as compared to the parent nucleoside or ▼ base ▼ compounds, and are thus useful cytotoxic, antiviral and antineoplastic agents.

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      FILE 'USPAT' ENTERED AT 09:12:50 ON 11 JUL 95)
L1          7647 S NUCLEOSID? OR NUCLEOTID?
L2       1081217 S MODIF? OR ANALOG?
L3          6634 S L1 AND L2
L4        641938 S BASE OR BASES
L5          5006 S L4 AND L3
L6          1582 S COVALENT? AND L5
L7           994 S HYBRIDIZ? AND L6
L8           317 S HYDROGEN(2W)BOND? AND L6
L9          1105 S L7 OR L8
L10          599 S (DIFFICULT? OR UNPREDICT? OR COMPLICAT?) AND L9
L11        70741 S 1982/FD
L12           31 S (L11 OR 1981/FD OR 1983/FD) AND L10
L13          967 S NUCLEOSID?(3A)MODIF? OR NUCLEOSID?(3A)ANALOG?
OR NUCLEOT ID?
L14          813 S L13 AND L4
L15          191 S COVALENT? AND L14 AND (DIFFICULT? OR UNPREDICT?
OR COMPL ICA

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d 112 cit,ab 1-31;d his

1. 5,169,941, Dec. 8, 1992, DNA sequences coding for the DR .beta.-chain locus of the human lymphocyte antigen complex and polypeptides, diagnostic typing processes and products related thereto; Bernard F. Mach, et al., 536/26.1; 435/69.3, 91.1, 91.41, 172.3, 240.2, 240.4, 252.31, 252.33, 252.34, 254.11, 254.2 [IMAGE AVAILABLE]

US PAT NO: 5,169,941 [IMAGE AVAILABLE] L12: 1 of 31

ABSTRACT:
DNA sequences coding for the DR-.beta.-chain locus of human lymphocyte antigen complex and diagnostic typing processes and products related thereto. DNA sequences that code for the .beta.-chain DR locus are useful in simple and efficient typing processes and products and for expression of polypeptides displaying an immunological or biological activity of the antigens of the HLA-DR .beta.-chains for use in diagnostic, preventive and therapeutic agents.

2. 4,816,567, Mar. 28, 1989, Recombinant immunoglobin preparations; Shmuel Cabilly, et al., 530/387.3; 435/69.6, 172.3, 252.3, 252.31, 252.33, 252.34, 320.1; 530/388.85, 866, 867; 930/10, 300; 935/10, 15, 29, 73 [IMAGE AVAILABLE]

US PAT NO: 4,816,567 [IMAGE AVAILABLE] L12: 2 of 31

ABSTRACT:
Altered and native immunoglobulins, including constant-variable region chimeras, are prepared in recombinant cell culture. The immunoglobulins contain variable regions which are immunologically capable of binding predetermined antigens. Methods are provided for refolding directly expressed immunoglobulins into immunologically active form.

3. 4,757,006, Jul. 12, 1988, Human factor VIII:C gene and recombinant methods for production; John J. Toole, Jr., et al., 435/69.6, 6, 172.3, 240.2, 320.1; 536/23.5; 930/100; 935/9, 11, 73 [IMAGE AVAILABLE]

US PAT NO: 4,757,006 [IMAGE AVAILABLE] L12: 3 of 31

ABSTRACT:
The protein having factor VIII:C procoagulant activity has been produced by culturing a cell transformed with a recombinant expression vector encoding the gene for that activity.

4. 4,740,461, Apr. 26, 1988, Vectors and methods for transformation of eucaryotic cells; Randal J. Kaufman, 435/69.1, 69.4, 69.6, 172.3, 212, 215, 240.2; 536/23.1, 24.1; 930/240; 935/32, 33, 56, 70 [IMAGE AVAILABLE]

US PAT NO: 4,740,461 [IMAGE AVAILABLE] L12: 4 of 31

ABSTRACT:
Eucaryotic cells cotransformed with product and selection genes

yield considerably greater quantities of product after a novel subcloning strategy is employed: Transformants are identified for product yield, cultured under selection pressure and the progeny screened for product yield. Novel transformation vectors contain directly ligated selection and product genes and/or eucaryotic promoters.

5. 4,724,202, Feb. 9, 1988, Use of non- • hybridizable • nucleic acids for the detection of nucleic acid • hybridization • ; Nanibhushan Dattagupta, et al., 435/6; 436/518, 811; 536/24.3, 25.32; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,724,202 [IMAGE AVAILABLE] L12: 5 of 31
ABSTRACT:
A detection probe comprising a • hybridizable • single stranded portion of nucleic acid connected with a non- • hybridizable • , single or double stranded nucleic acid portion, the non- • hybridizable • portion preferably including a recognition site for a particular protein.

6. 4,719,176, Jan. 12, 1988, Enzyme-free diagnostic binding reagents; Irving M. Klotz, 435/6, 810; 436/501, 537, 544, 547, 808; 536/24.3, 25.32 [IMAGE AVAILABLE]

US PAT NO: 4,719,176 [IMAGE AVAILABLE] L12: 6 of 31
ABSTRACT:
An enzyme-free diagnostic reagent, methods of its use and diagnostic systems containing that reagent are disclosed. The enzyme-free diagnostic reagent comprises an enzyme-free catalyst coupled by a linking group to a first binding agent, binds in aqueous medium to a second binding moiety to form a binding complex, and indicates the amount of second binding moiety present in the complex by means of its catalytic reactivity with co-reactant molecules.

7. 4,717,653, Jan. 5, 1988, Method for identifying and characterizing organisms; John A. Webster, Jr., 435/6, 6, 35, 39, 172.3, 803; 436/501; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,717,653 [IMAGE AVAILABLE] L12: 7 of 31
ABSTRACT:
A method of characterizing an unknown organism which comprises comparing the chromatographic pattern of restriction endonuclease-digester DNA from the unknown organism, which digested DNA has been • hybridized • or reassociated with ribosomal RNA information-containing nucleic acid from or derived from a known probe organism, with at least two equivalent chromatographic patterns, each one of the equivalent chromatographic patterns defining a known different organism species; and establishing the species of the unknown organism by means of a conserved set of ribosomal RNA sequence-containing restriction fragments present in the chromatographic pattern of

the unknown organism.

8. 4,711,955, Dec. 8, 1987, ▼ Modified ▼ ▼ nucleotides ▼ and methods of preparing and using same; David C. Ward, et al., 536/25.32, 25.6, 26.6 [IMAGE AVAILABLE]

US PAT NO: 4,711,955 [IMAGE AVAILABLE] L10: 8 of 31
ABSTRACT:
Compounds having the structure: ##STR1## wherein B represents a purine, 7-deazapurine, or pyrimidine moiety ▼ covalently ▼ bonded to the C.sup.1' -position of the sugar moiety, provided that when B is purine or 7-deazapurine, it is attached at the N.sup.9 -position of the purine or 7-deazapurine and when B is pyrimidine, it is attached at the N.sup.1 -position;
wherein A represents a moiety consisting of at least three carbon atoms which is capable of forming a detectable complex with a polypeptide when the compound is incorporated into a double-stranded ribonucleic acid, deoxyribonucleic acid duplex, or DNA-RNA hybrid;
wherein the dotted line represents a chemical linkage joining B and A, provided that if B is purine, the linkage is attached to the 8-position of the purine, if B is 7-deazapurine, the linkage is attached to the 7-position of the deazapurine, and if B is pyrimidine, the linkage is attached to the 5-position of the pyrimidine and
wherein each of x, y and z represents ##STR2## either directly, or when incorporated into oligo- and polynucleotides, provide probes which are widely useful.
Applications include detection and localization of polynucleotide sequences in chromosomes, fixed cells, tissue sections, and cell extracts. Specific applications include chromosomal karyotyping, clinical diagnosis of nucleic acid-containing etiological agents, e.g. bacteria, viruses, or fungi, and diagnosis of genetic disorders.

9. 4,672,032, Jun. 9, 1987, Dental enamel production; Harold C. Slavkin, et al., 435/68.1; 424/49, 52, 57, 602, 676; 435/69.1, 212, 219; 530/350; 930/10 [IMAGE AVAILABLE]

US PAT NO: 4,672,032 [IMAGE AVAILABLE] L10: 9 of 31
ABSTRACT:
Methods are provided for the formation of dental enamel crystals in biosynthetic matrix form by the nucleation of calcium solutions with enamel proteins and for the use of such enamel crystals as restorative material.

10. 4,661,450, Apr. 28, 1987, Molecular cloning of RNA using RNA ligase and synthetic oligonucleotides; Tomas Kempe, et al., 435/91.41, 172.3, 320.1 [IMAGE AVAILABLE]

US PAT NO: 4,661,450 [IMAGE AVAILABLE] L10: 10 of 31

ABSTRACT:
Methods and compositions for the insertion and molecular cloning of RNA in DNA cloning vectors are described. RNA molecules to be cloned are • modified • by the ligation of oligonucleotide linkers onto the termini of the RNA molecule using T4 RNA ligase. Such linkers may be composed of DNA, RNA, or mixtures of each and facilitate the insertion and ligation of the RNA species into a DNA cloning vector. The resulting recombinant vectors are used to transform host cells which provide for the generation of multiple DNA copies of the RNA molecule.

11. 4,652,639, Mar. 24, 1987, Manufacture and expression of structural genes; Yitzhak Stabinsky, 435/91.52, 69.4, 91.53, 172.3, 320.1; 536/23.1; 930/80; 935/16, 17 [IMAGE AVAILABLE]

US PAT NO: 4,652,639 [IMAGE AVAILABLE] L12: 11 of 31
ABSTRACT:
Described are rapid and highly efficient procedures for the total synthesis of linear, double stranded DNA sequences of up to about 200 • base • pairs, which sequences may comprise entire structural genes. Illustratively disclosed is the preparation and expression of manufactured genes, including fusion genes, capable of directing synthesis of human .beta.-endorphin and of proteins which differ from human .beta.-endorphin in terms of the identity or relative position of one or more amino acids. Manufactured genes preferably include codons selected from among alternative codons specifying the same amino acid on the basis of preferential expression in a projected host microorganism (e.g., E. coli) to be transformed.

12. 4,652,525, Mar. 24, 1987, Recombinant bacterial plasmids containing the coding sequences of insulin genes; William J. Rutter, et al., 435/252.33, 172.3, 320.1, 849; 930/10 [IMAGE AVAILABLE]

US PAT NO: 4,652,525 [IMAGE AVAILABLE] L12: 12 of 31
ABSTRACT:
A recombinant procaryotic microorganism containing the gene coding for insulin.

13. 4,650,770, Mar. 17, 1987, Energy absorbing particle quenching in light emitting competitive protein binding assays; Yen-Ping Liu, et al., 436/503, 533, 534, 537, 546, 805 [IMAGE AVAILABLE]

US PAT NO: 4,650,770 [IMAGE AVAILABLE] L12: 13 of 31
ABSTRACT:
Assays are provided employing particles and absorbent particles, wherein the absorbent particles substantially inhibit fluorescence when bound to the fluorescent particles through specific non- • covalent • binding.

14. 4,642,334, Feb. 10, 1987, Hybrid DNA prepared binding composition; Kevin W. Moore, et al., 530/387.3; 424/133.1, 178.1, 183.1, 801; 435/7.92, 7.94, 69.6, 172.3, 172.3, 317.1; 436/547; 530/389.8, 391.3, 391.7, 808, 809, 866, 867; 930/10, 300 [IMAGE AVAILABLE]

US PAT NO: 4,642,334 [IMAGE AVAILABLE] L12: 14 of 31

ABSTRACT:

Proteinaceous binding compositions are prepared employing hybrid DNA techogy, where the variable region polypeptides of immunoglobulins are substantially reproduced to provide relatively small protein molecules having binding specificity and lacking the undesirable aspects of the heavy regions of immunoglobulins. The compositions find a wide range of use, particularly for physiological purposes for diagnosis and therapy. The binding compositions may be • modified • by labeling with radioisotopes, fluoresoers, and toxins for specific applications in diagnosis or therapy.

15. 4,634,665, Jan. 6, 1987, Processes for inserting DNA into eucaryotic cells and for producing proteinaceous materials; Richard Axel, et al., 435/69.1, 69.3, 69.4, 69.5, 69.51, 69.52, 69.6, 172.3, 240.3, 811, 949; 536/23.1, 23.51, 23.52; 935/27, 31, 34, 56, 58, 70 [IMAGE AVAILABLE]

US PAT NO: 4,634,665 [IMAGE AVAILABLE] L12: 15 of 31

ABSTRACT:

The present invention relates to processes for inserting DNA into eucaryotic cells, particularly DNA which includes a gene or genes coding for desired proteinaceous materials for which no selective criteria exist. The insertion of such DNA molecules is accomplished by cotransforming eucaryotic cells with such DNA together with a second DNA which corresponds to a gene coding for a selectable marker. This invention also concerns processes for producing proteinaceous materials such as insulin, interferon protein, growth hormone and the like which involve cotransforming eucaryotic cells with DNA which codes for these proteinaceous materials, growing the contransformed cells for production of the proteinaceous material and recovering the proteinaceous material so produced.

The invention further relates to processes for inserting into eucaryotic cells a multiplicity of DNA molecules which includes genes coding for desired proteinaceous materials. The insertion of multiple copies of desired genes is accomplished by cotransformation with the desired genes and with amplifiable genes for a dominant selectable marker in the presence of successively higher amounts of an inhibitor. Alternatively, the insertion of multiple copies of desired genes is accomplished by transformation using DNA molecules formed by ligating a DNA molecule including the desired gene to a DNA molecule which includes an amplifiable gene coding for a dominant selectable phenotype such as a gene associated with resistance to a drug in the presence of successively higher amounts of an agent such as a

drug against which the gene confers resistance so that only those eucaryotic cells into which multiple copies of the amplifiable gene have been inserted survive. Eucaryotic cells into which multiple copies of the amplifiable gene have been inserted additionally include multiple copies of the desired gene and may be used to produce multiple copies of proteinaceous molecules. In this way otherwise rare proteinaceous materials may be obtained in higher concentrations than are obtainable using conventional techniques.

16. 4,629,692, Dec. 16, 1986, Immunoassay for nonenzymatically glucosylated proteins and protein fragments an index of glycemia; Kenneth J. Dean, 435/7.7, 7.71, 7.72, 7.9, 188, 810, 961, 975; 436/67, 518, 811, 822, 823; 530/322, 389.3, 389.6, 389.8 [IMAGE AVAILABLE]

US PAT NO: 4,629,692 [IMAGE AVAILABLE] L12: 16 of 31

ABSTRACT:

An immunoassay method and reagent system for determining nonenzymatically glucosylated proteins and protein fragments in a biological fluid based on the specific binding of such proteins and fragments with anti(Amadori-rearranged glucose), e.g., antibodies which selectively recognize the rearranged deoxyfructose form of glucose resulting when proteins are nonenzymatically glucosylated. The antibodies are raised against an immunogen comprising an immunogenic carrier material bearing 1-deoxy-1-fructosyl residues or conformers of such residues. Measurement of nonenzymatically glucosylated proteins and fragments thereof provides a useful index of blood glucose levels.

17. 4,593,002, Jun. 3, 1986, Viruses with recombinant surface proteins; Renato Dulbecco, 435/172.3; 424/199.1, 217.1, 224.1, 233.1; 435/69.1, 69.3, 91.41, 235.1, 239, 317.1; 536/23.1; 935/12, 31, 32, 65 [IMAGE AVAILABLE]

US PAT NO: 4,593,002 [IMAGE AVAILABLE] L12: 17 of 31

ABSTRACT:

Foreign protein segments having specific medically or commercially useful biological functions are incorporated in surface proteins of viruses. The viruses with the incorporated protein segments are convenient agents for introducing the protein segments into animals, such as humans, and are thus useful as vaccines. Small segments of an original protein exhibiting desired functions are identified, and a DNA fragment having a ▼ nucleotide ▼ ▼ base ▼ sequence encoding that segment of the protein is isolated from an organism or synthesized chemically. The isolated DNA fragment is inserted into the DNA genome of a virus in a manner such that the inserted DNA fragment expresses itself as the foreign segment of a surface viral protein and in such a way that neither the function of the protein segment nor the function of any viral protein critical for viral replication is impaired.

18. 4,587,044, May 6, 1986, Linkage of proteins to nucleic acids; Paul S. Miller, et al., 530/322; 424/179.1; 435/6, 177, 180, 181; 530/358, 391.9; 536/23.1, 25.32, 25.5, 26.12, 26.14, 26.26 [IMAGE AVAILABLE]
US PAT NO: 4,587,044 [IMAGE AVAILABLE] L12: 18 of 31
ABSTRACT:
A nucleic acid-protein conjugate which is specific with respect to a selected living cell is prepared by linking said nucleic acid to a protein specific to said living cell.

19. 4,563,419, Jan. 7, 1986, Detection of microbial nucleic acids by a one-step sandwich ▼ hybridization ▼ test; Tuula M. Ranki, et al., 435/6, 4, 5, 172.3, 189, 910; 436/501, 504, 804, 808, 811, 823; 536/23.7, 24.32; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,563,419 [IMAGE AVAILABLE] L12: 19 of 31
ABSTRACT:
This invention relates to a kit for the detection of microbial nucleic acids and a method for identifying the nucleic acids using a one-step sandwich ▼ hybridization ▼ technique. The technique requires two complementary nucleic acid reagents for each microbe or group of microbes to be identified.

20. 4,562,159, Dec. 31, 1985, Diagnostic test for hepatitis B virus; David A. Shafritz, 435/5; 206/569; 435/6, 172.3, 317.1, 949; 436/504, 804, 808, 810, 811, 815, 820; 536/24.3, 24.32, 25.32; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,562,159 [IMAGE AVAILABLE] L12: 20 of 31
ABSTRACT:
A method and test kit are disclosed for detecting the presence of hepatitis B virus in a test specimen containing at least a portion of the DNA of the virus. A test reagent comprises cloned hepatitis B virus-DNA that has been repurified by treatment with a restriction enzyme and labelled to high specific activity with a radioactive label. The sample to be tested is fixed to a solid matrix, incubated in the presence of the test reagent under ▼ hybridization ▼ conditions and detected by ▼ hybridization ▼ to the labelled DNA probe. The uncombined HBV-DNA (labelled) is removed from the substrate, and the ▼ hybridized ▼ HBV-DNA determined by scintillation counting or by autoradiography of the substrate.

21. 4,530,904, Jul. 23, 1985, Method for conferring bacteriophage resistance to bacteria; Charles L. Hershberger, et al., 435/172.3, 69.1, 69.3, 69.4, 69.5, 69.51, 69.52, 69.6, 91.41, 252.2, 252.3, 252.31, 252.33, 252.34, 252.35, 320.1, 949; 536/23.2, 24.2; 930/10, 180; 935/29, 72, 73, 83 [IMAGE AVAILABLE]

US PAT NO: 4,530,904 [IMAGE AVAILABLE] L12: 21 of

31
ABSTRACT:
A novel method for protecting a bacterium from a naturally occurring bacteriophage and the cloning vectors and transformants for carrying out the aforementioned method are disclosed.

22. 4,508,826, Apr. 2, 1985, Bacteriophage DNA cloning vector TG1 and microorganisms containing TG1; Forrest Foor, et al., 435/320.1, 172.3, 239, 252.3, 252.35; 935/31, 75 [IMAGE AVAILABLE]

US PAT NO: 4,508,826 [IMAGE AVAILABLE] L12: 22 of 31
ABSTRACT:
Disclosed is the novel bacteriophage TG1, TG1 derivatives, and the corresponding genome or nucleic acid components of such bacteriophages and derivatives of such genome, which are useful as DNA cloning vectors into organisms, such as bacteria, for example, Streptomyces cattleya NRRL 8057; portions of such phage genome are additionally useful as adjuncts in recombinant DNA cloning procedures, for example: (1) to permit the maintenance of cloned DNA in the host, either in an integrated state or as an autonomous element; (2) to serve as promoters for increasing expression of endogenous or foreign genes wherein said promoters are ligated to such genes or otherwise serve as promoters; and (3) to serve as regulatory elements for achieving control over endogenous and foreign gene expression; as cloning vectors, TG1, its deletion mutants, and other derivatives serve for the amplification and transfer of DNA sequences (genes) coding for useful functions, for example, genes necessary for the production of the antibiotic thienamycin, or genes necessary for the production of hepatitis B antigen, and of DNA sequences which are useful per se, for example, distinct plasmid vectors which are inherently useful; such ▼ modified ▼ cloning vectors (hybrid DNA molecules comprising the TG1 genome or portions thereof and foreign DNA sequence) are introduced into the recipient organism by infection, transfection or transformation; wherein the hybrid DNA functions in an integrated mode, in a lytic (vegetative phase) mode and/or in a plasmid mode. Also disclosed are microorganisms comprising TG1 prophage and deletion and hybride (chimeric) derivatives thereof; and microorganisms comprising hybrid (chimeric) phage-plasmids and derivatives thereof.

23. 4,493,929, Nov. 20, 1984, Liposomes with glycolipid-linked antibodies; Frank C. Szoka, 436/533; 435/7.9, 8, 966; 436/512, 532, 534, 548, 800, 803, 819, 828, 829 [IMAGE AVAILABLE]

US PAT NO: 4,493,929 [IMAGE AVAILABLE] L12: 23 of 31
ABSTRACT:
Lipid vesicles, labelled with encapsulated reporter compositions and bound to antibodies comprise a new class of immunoreagent, useful in immunoassays for ligands.

24. 4,466,917, Aug. 21, 1984, Malaria vaccine; Ruth S. Nussenzweig, et al., 530/350; 424/268.1; 435/69.3, 69.7, 172.2, 172.3; 530/806, 808; 935/6, 22, 45, 65, 109 [IMAGE AVAILABLE]

US PAT NO: 4,466,917 [IMAGE AVAILABLE] L12: 24 of 31
ABSTRACT:

The present invention provides antisera and monoclonal antibodies directed against the sporozoite stage of the malaria parasite capable of providing protection against infection in both animals and humans. The invention further provides a purified antigen derived from sporozoites of the malaria parasite, the antigen being suitable for use as a vaccine against malarial infections in both animals and humans. The invention further provides means for preparing said antigen and a vaccine comprising said antigen.

25. 4,460,689, Jul. 17, 1984, DNA Cloning vector TG1, derivatives, and processes of making; Forrest Foor, et al., 435/172.3, 69.1, 69.3, 239, 252.35, 320.1, 886; 935/9, 12, 23, 31, 41, 73, 75 [IMAGE AVAILABLE]
US PAT NO: 4,460,689 [IMAGE AVAILABLE] L12: 25 of 31
ABSTRACT:
Disclosed is the novel bacteriophage TG1, TG1 derivatives, and the corresponding genome or nucleic acid components of such bacteriophages and derivatives of such genome, which are useful as DNA cloning vectors into organisms, such as bacteria, for example, Streptomyces cattleya NRRL 8057; portions of such phage genome are additionally useful as adjuncts in recombinant DNA cloning procedures, for example: (1) to permit the maintenance of cloned DNA in the host, either in an integrated state or as an autonomous element; (2) to serve as promoters for increasing expression of endogenous or foreign genes wherein said promoters are ligated to such genes or otherwise serve as promoters; and (3) to serve as regulatory elements for achieving control over endogenous and foreign gene expression; as cloning vectors, TG1, its deletion mutants, and other derivatives serve for the amplification and transfer of DNA sequences (genes) coding for useful functions, for example, genes necessary for the production of the antibiotic thienamycin, or genes necessary for the production of hepatitis B antigen, and of DNA sequences which are useful per se, for example, distinct plasmid vectors which are inherently useful; such • modified • cloning vectors (hybrid DNA molecules comprising the TG1 genome or portions thereof and foreign DNA sequence) are introduced into the recipient organism by infection, transfection or transformation; wherein the hybrid DNA functions in an integrated mode, in a lytic (vegetative phase) mode and/or in a plasmid mode. Also disclosed are microorganisms comprising TG1 prophage and deletion and hybrid (chimeric) derivatives thereof; and microorganisms comprising hybrid (chimeric) phage-plasmids and derivatives thereof.

26. 4,451,566, May 29, 1984, Methods and apparatus for

enzymatically producing ethanol; Donald B. Spencer, 435/162, 175, 188, 813, 814, 815, 819 [IMAGE AVAILABLE]

US PAT NO: 4,451,566 [IMAGE AVAILABLE] L12: 26 of 31
ABSTRACT:
Methods and apparatus are provided for the enzymatic production of ethanol from fermentable sugars. A complete sequence of enzymes for catalyzing the conversion of fermentable sugars to ethanol is retained in a plurality of reaction zones. Fermentable sugar solution is sequentially passed through the zones, and ethanol is recovered from the last zone. Necessary coenzymes and cofactors are added to the solution in the various zones, and means are provided for recovering and, if necessary, • modifying • the coenzymes prior to reintroduction in the various zones.
27. 4,447,538, May 8, 1984, Microorganism containing gene for human chorionic somatomammotropin; Howard M. Goodman, et al., 435/252.33, 172.3; 930/120; 935/13, 19, 21, 29, 73 [IMAGE AVAILABLE]

US PAT NO: 4,447,538 [IMAGE AVAILABLE] L12: 27 of 31
ABSTRACT:
A microorganism containing a recombinant DNA transfer vector having the coding sequences for human chorionic somatomammotropin.

28. 4,440,859, Apr. 3, 1984, Method for producing recombinant bacterial plasmids containing the coding sequences of higher organisms; William J. Rutter, et al., 435/91.41, 69.1, 69.4, 172.3, 320.1; 935/4, 13, 29 [IMAGE AVAILABLE]

US PAT NO: 4,440,859 [IMAGE AVAILABLE] L12: 28 of 31
ABSTRACT:
Microorganism having a gene derived from a higher organism is produced by isolating cells from a higher organism containing messenger RNA, extracting the messenger RNA, synthesizing a double stranded cDNA using the messenger RNA as a template, inserting the cDNA into a plasmid and transforming a microorganism with the resultant recombinant plasmid.
29. 4,407,948, Oct. 4, 1983, Purification of • nucleotide • sequences suitable for expression in bacteria; Howard M. Goodman, et al., 435/91.52, 91.53, 172.3, 270; 536/23.1; 930/10, 120; 935/19, 29 [IMAGE AVAILABLE]

US PAT NO: 4,407,948 [IMAGE AVAILABLE] L12: 29 of 31
ABSTRACT:
A method for purifying a DNA fragment of specific desired • nucleotide • sequence containing a restriction site, from a population of DNA molecules homogeneous in length by endonuclease cleavage and fractionation.

30. 4,391,904, Jul. 5, 1983, Test strip kits in immunoassays and compositions therein; David J. Litman, et al., 435/7.91; 422/55, 56; 435/188, 805, 810, 975; 436/536, 537 [IMAGE AVAILABLE]

US PAT NO: 4,391,904 [IMAGE AVAILABLE] L12: 30 of 31

ABSTRACT:
An assay method and compositions are provided for determining the presence of an analyte in a sample. The analyte is a member of an immunological pair (mip) of immunogens--ligand and receptor. The method has two basic elements: a solid surface to which one of the members of the immunological pair is bonded and a signal producing system, which includes a catalytic member bonded to a mip, which signal producing system results in a measurable signal on said solid surface related to the amount of analyte in the medium. The signal generating compound is produced without separation of the catalyst labeled mip bound to the solid surface from the catalyst labeled mip free in solution. In a preferred embodiment, an enzyme is bonded to a mip which acts in conjunction with a solute to produce a signal generating product which binds preferentially to the solid surface when the enzyme is bound to the surface, resulting in a signal which is readily differentiated from signal generating compound produced by the catalyst and solute in the bulk solution.

31. 4,379,843, Apr. 12, 1983, Immobilization of polynucleotides and polypeptides with tritylated polysaccharides; Peter Cashion, 435/178, 91.3, 179, 181, 814, 815; 935/18, 19, 20, 21, 78 [IMAGE AVAILABLE]

US PAT NO: 4,379,843 [IMAGE AVAILABLE] L12: 31 of 31

ABSTRACT:
Polynucleotides and Polypeptides are immobilized and/or isolated by using a triphenylmethyl ether derivative of polysaccharides in hydrated form.

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     (FILE 'USPAT' ENTERED AT 09:12:50 ON 11 JUL 95)
L1          7647 S NUCLEOSID? OR NUCLEOTID?
L2       1181217 S MODIF? OR ANALOG?
L3          6634 S L1 AND L2
L4        641939 S BASE OR BASES
L5          5006 S L4 AND L3
L6          1592 S COVALENT? AND L5
L7           994 S HYBRIDIZ? AND L6
L8           317 S HYDROGEN(2W)BOND? AND L6
L9          1106 S L7 OR L8
L10          599 S (DIFFICULT? OR UNPREDICT? OR COMPLICAT?) AND L9
L11        70741 S 1980/FD
L12           31 S (L11 OR 1981/FD OR 1983/FD) AND L10

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(1)  5,430,139, Jul. 4, 1995, Hydroxyl-protecting groups attached
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to cytidine nucleotide compounds which are orthogonally removable; Michael S. Urdea, et al., 536/26.9, 29.5, 29.51, 29.52 [IMAGE AVAILABLE]

US PAT NO: 5,430,138 [IMAGE AVAILABLE] L15: 1 of 191

ABSTRACT:
Hydroxyl-protecting groups orthogonally removable by reduction with a liquid reducing agent are disclosed. The novel hydroxyl-protecting groups are particularly useful in the chemical synthesis of linear and branched oligonucleotide structures, as they are readily removed from the protected molecule with mild reagents such as dithionite. Examples of such hydroxyl-protecting groups include the 2-methylene-9,10-anthraquinone (Maq) carbonate ester and the p-nitrobenzyl carbonate ester.

2. 5,428,147, Jun. 27, 1995, Octopine T-DNA promoters; Richard F. Barker, et al., 536/24.1; 435/69.1, 70.1, 172.3, 240.4, 252.3, 320.1 [IMAGE AVAILABLE]

US PAT NO: 5,428,147 [IMAGE AVAILABLE] L15: 2 of 191

ABSTRACT:
The sequence of the T-DNA of the octopine-type Ti plasmid found in Agrobacterium tumefaciens ATCC 15955 is disclosed. Fourteen open reading frames bounded by eukaryotic promoters, ribosome binding sites, and polyadenylation sites were found. The use of promoters and polyadenylation sites from pTi15955 to control expression of foreign structural genes is taught, using as examples the structural genes for the Phaseolus vulgaris storage protein phaseolin, P. vulgaris lectin, thaumatin, and Bacillus thuringiensis crystal protein. Vectors useful for manipulation of sequences of the structural genes and T-DNA are also provided.

3. 5,427,929, Jun. 27, 1995, Method for reducing carryover contamination in an amplification procedure; Rodney M. Richards, et al., 435/91.2, 6; 935/77, 78 [IMAGE AVAILABLE]

US PAT NO: 5,427,929 [IMAGE AVAILABLE] L15: 3 of 191

ABSTRACT:
The present invention provides an efficient and economical method for reducing carryover contamination in an amplification procedure. The method of the present invention enables background caused by contaminant amplification product to be reduced or eliminated through the incorporation of at least one modification into the amplification product. The modified amplification product is readily distinguishable from the target sequence in a test sample. Prior to amplifying the target in a new test sample, the sample may be treated to selectively cleave the contaminant amplification product so that it cannot be amplified in the new sample.

4. 5,424,395, Jun. 13, 1995, Antimicrobial peptides active

against plant pathogens; Newell F. Bascomb, et al., 530/326, 300 [IMAGE AVAILABLE]
US PAT NO: 5,424,395 [IMAGE AVAILABLE] L15: 4 of 191
ABSTRACT:
The present invention relates to a number of peptides which have antimicrobial activity and which are useful in retarding plant pathogens. In addition, compounds in accordance with the present invention may have improved resistance to degradation by plant proteases, and/or sufficiently low phytotoxicity to render them likely candidates for use in conjunction with plants. The present invention also relates to oligonucleotides which are capable of expressing the aforementioned peptides. Also provided hereby is a process of retarding the growth of plant pathogens using the compounds of the present invention as well as a screening method and screening reagent useful in determining the proteolytic degradation resistance of a known compound.

5. 5,424,188, Jun. 13, 1995, Amplified hybridization assay; Robert J. Schneider, et al., 435/6; 536/24.3; 935/77, 78 [IMAGE AVAILABLE]
US PAT NO: 5,424,188 [IMAGE AVAILABLE] L15: 5 of 191
ABSTRACT:
A kit for an amplified hybridization assay is described in which a family of signal-generating secondary probes bind to a primary probe that hybridizes to the target sequence of interest. Thus, an enormously amplified signal is generated by the hybridization event. The assay can be used for a variety of laboratory and clinical purposes and is automatable. A hybridization assay kit is also described. The kit is used for the detection of a target nucleotide sequence. One embodiment of the kit includes a plurality of secondary probes, each secondary probe capable of binding to a distinct binding site of the primary probe.
6. 5,422,266, Jun. 6, 1995, Recombinant DNA vectors capable of expressing apoaequorin; Milton J. Cormier, et al., 435/252.3, 69.1, 172.3, 252.33, 320.1; 536/23.5; 935/11, 73 [IMAGE AVAILABLE]
US PAT NO: 5,422,266 [IMAGE AVAILABLE] L15: 6 of 191
ABSTRACT:
A gene which codes for the protein apoaequorin is disclosed alone with recombinant DNA vectors containing this gene. Homogeneous peptides having the bioluminescence properties of natural, mixed apoaequorin are also disclosed.

7. 5,420,115, May 30, 1995, Method for the treatment of protozoa infections with 2.sup.1 -deoxy-2.sup.1 -fluoropurine nucleosides; Sylvia M. Tisdale, et al., 514/46, 45; 536/27.61, 27.81 [IMAGE AVAILABLE]
US PAT NO: 5,420,115 [IMAGE AVAILABLE] L15: 7 of 191
ABSTRACT:
A method for treating two specific protozoal infections,

Trichomonas vaginalis and Giardia lamblia, comprising the administration to a mammal in need thereof one of the following purine nucleosides:
2,6-diamino-9-(2-deoxy-2-fluoro-.beta.-D-ribofuranosyl -9H-purine
2-amino-9-(2-deoxy-2-fluoro-.beta.-D-ribofuranosyl)-9H-purine
2-amino-9-(2-deoxy-2-fluoro-.beta.-D-ribofuranosyl)-6-methoxy-9H-purine.
8. 5,417,971, May 23, 1995, Vaccines for Actinobacillus pleuropneumoniae; Andrew A. Potter, et al., 424/256.1, 234.1; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,417,971 [IMAGE AVAILABLE] L15: 8 of 191
ABSTRACT:
Novel vaccines for use against Actinobacillus pleuropneumoniae are disclosed. The vaccines contain at least one A. pleuropneumoniae transferrin binding protein and/or one A. pleuropneumoniae cytolysin and/or one A. pleuropneumoniae APP4. Also disclosed are DNA sequences encoding these proteins, vectors including these sequences and host cells transformed with these vectors. The vaccines can be used to treat or prevent porcine respiratory infections.

9. 5,416,203, May 16, 1995, Steroid modified oligonucleotides; Robert L. Letsinger, 536/25.34, 5, 25.31, 25.33 [IMAGE AVAILABLE]

US PAT NO: 5,416,203 [IMAGE AVAILABLE] L15: 9 of 191
ABSTRACT:
An oligonucleotide conjugated to a steroid the oligonucleotide comprising: ##STR1## wherein A is selected from the group consisting of an aliphatic alkyl, branched aliphatic alkyl and an alkyl (branched) chain of 2 to 18 carbon atoms, R is selected from the group consisting of H and lower alkyl up to 12 carbon atoms; B is a naturally occurring • base • , the steroid is bound to the oligonucleotide utilizing the naturally occurring • bases • through an (-oxycarbonyl-amino)-decylamine- moiety, and NUC is an oligonucleotide.

10. 5,416,016, May 16, 1995, Method for enhancing transmembrane transport of exogenous molecules; Philip S. Low, et al., 435/240.1; 424/450; 435/172.3, 240.4, 243; 514/2, 44 [IMAGE AVAILABLE]
US PAT NO: 5,416,016 [IMAGE AVAILABLE] L15: 10 of 191
ABSTRACT:
A method is provided for enhancing transmembrane transport of exogenous molecules. The method comprises contacting a membrane of a living cell with a complex formed between said molecules and ligands selected from biotin, biotin analogs and other biotin receptor-binding ligands, and/or folic acid, folate analogs and other folate receptor-binding ligands to initiate receptor mediated transmembrane transport of the ligand complex. The method is used for the efficient delivery of peptides, proteins,

nucleic acids and other compounds capable of modifying cell function into plant, animal, yeast, and bacterial cells.

11. 5,411,947, May 2, 1995, Method of converting a drug to an orally available form by ▼ covalently ▼ bonding a lipid to the drug; Karl Y. Hostetler, et al., 514/43, 2, 12, 18, 50, 192, 199, 200, 885 [IMAGE AVAILABLE]

US PAT NO: 5,411,947 [IMAGE AVAILABLE] L15: 11 of 191

ABSTRACT:

The oral delivery of many classes of drugs is facilitated by converting drugs having suitable functional groups to 1-O-alkyl-, 1-O-acyl-, 1-S-acyl, and 1-S-alkyl-sn-glycero-3-phosphate derivatives. The method confers the ability to be absorbed through the digestive tract to drugs that are not orally bioavailable in the non-derivatized state, and enhances the effectiveness of drugs that are poorly absorbed or rapidly eliminated. The method provides orally bioavailable lipid prodrugs of pharmaceutical compounds having diverse physiological activities, including anticancer and antiviral agents, anti-inflammatory agents, antihypertensives and antibiotics. Potency of the lipid prodrugs is comparable to that of the corresponding non-derivatized drugs.

12. 5,411,876, May 2, 1995, Use of grease or wax in the polymerase chain reaction; Will Bloch, et al., 435/91.2; 206/219, 569, 569; 435/6; 935/16, 17, 18 [IMAGE AVAILABLE]

US PAT NO: 5,411,876 [IMAGE AVAILABLE] L15: 12 of 191

ABSTRACT:

Improvements to the polymerase chain reaction (PCR), a process for in vitro enzymatic amplification of specific nucleic acid sequences, can be achieved by changing the way that PCR reagents are mixed and the enzymatic reaction is started and by the replacement of mineral oil, commonly used as a vapor barrier to minimize solvent evaporation, by a grease or wax. The use of such mixtures allows for the delay of reagent mixing until the first heating step of a PCR amplification, thereby reducing the enzymatic generation of nonspecific products which occurs when a complete mixture of PCR reagents, with or without test sample, stands at room temperature or below. These mixtures increase the shelf-life of PCR reagents and increase protection of the laboratory environment against contamination by PCR product.

13. 5,410,068, Apr. 25, 1995, Succinimidyl trityl compounds and a process for preparing same; James M. Ocull, et al., 549/545; 536/25.31; 548/215 [IMAGE AVAILABLE]

US PAT NO: 5,410,068 [IMAGE AVAILABLE] L15: 13 of 191

ABSTRACT:

The invention pertains to compounds and methods for the reversible modification of natural products, biopolymers or

synthons for natural products or biopolymers, such as nucleosides, ▼ nucleotides ▼ , and oligonucleosides. The ▼ modification ▼ enables one to perform a variety of chemistries on these compounds, yet can be removed to regenerate functional groups on the natural products, biopolymer or synthon of interest.

14. 5,409,837, Apr. 25, 1995, Modified unF-13 protein and gene; Charles S. Levings, III, et al., 435/320.1, 69.1, 172.3; 530/370, 376; 536/23.6 [IMAGE AVAILABLE]

US PAT NO: 5,409,837 [IMAGE AVAILABLE] L15: 14 of 191
ABSTRACT:
A unf. 13 protein and gene encoding it are disclosed which confer sensitivity to B. maydis T toxin and the insecticide methomyl, in cells carrying the gene and expressing the protein. Toxin sensitivity domains of the protein have been identified wherein a modification yields a toxin-insensitive product.

15. 5,409,818, Apr. 25, 1995, Nucleic acid amplification process; Cheryl Davey, et al., 435/91.21, 6, 91.2 [IMAGE AVAILABLE]

US PAT NO: 5,409,818 [IMAGE AVAILABLE] L15: 15 of 191
ABSTRACT:
This invention relates to a process for amplifying a specific nucleic acid sequence. The process involves synthesizing single-stranded RNA, single-stranded DNA and double-stranded DNA. The single-stranded RNA is a first template for a first primer, the single-stranded DNA is a second template for a second primer, and the double stranded DNA is a third template for synthesis of a plurality of copies of the first template. A sequence of the first primer or the second primer is complementary to a sequence of the specific nucleic acid and a sequence of the first primer or the second primer is homologous to a sequence of the specific nucleic acid. The amplification process may be used to increase the quantity of the specific nucleic acid sequence to allow detection, or to increase the purity of the specific nucleic acid sequence as a substitute for conventional cloning methodology.

16. 5,408,039, Apr. 18, 1995, Nonnatural apolipoprotein B-100 peptides and apolipoprotein B-100-apolipoprotein A-I fusion peptides; Richard S. Smith, et al., 530/359; 435/7.1; 536/23.5 [IMAGE AVAILABLE]
US PAT NO: 5,408,039 [IMAGE AVAILABLE] L15: 16 of 191
ABSTRACT:
Methods and compositions are described for determining the level of low density lipoproteins (LDL) in plasma. Native apoprotein B-100 (apo B-100) present in LDL particles is immunologically mimicked by a polypeptide of the invention. A polypeptide includes an amino acid residue sequence corresponding to a pan

epitope region of the target apoprotein. A preferred polypeptide is a fusion protein that simultaneously mimics native apo B-100 and native apo A-I. Improved assay systems and methods for determining HDL and LDL levels in a body fluid sample are also described.

17. 5,405,952, Apr. 11, 1995, DNA sequence encoding nonglycosylated analogs of human colony stimulating factors; Michael Deeley, et al., 536/23.5; 435/69.5, 69.9, 172.3, 235.1, 252.3, 320.1; 530/350; 935/10, 28, 56, 61, 69 [IMAGE AVAILABLE]

US PAT NO: 5,405,952 [IMAGE AVAILABLE] L15: 17 of 191
ABSTRACT:
An analog human colony stimulating factor (hCSF) is disclosed, comprising a mutant amino acid sequence which is substantially homologous to the native sequence of an hCSF having at least one N-glycosylation site, wherein the mutant sequence comprises at least one amino acid substitution, deletion or insertion inactivating the N-glycosylation site.

18. 5,405,939, Apr. 11, 1995, Sequence-specific binding polymers for duplex nucleic acids; James E. Summerton, et al., 528/406; 525/54.1, 54.3, 383, 384, 385; 528/245, 403, 417, 420, 422, 423, 425 [IMAGE AVAILABLE]

US PAT NO: 5,405,939 [IMAGE AVAILABLE] L15: 18 of 191
ABSTRACT:
The present invention describes a polymer composition effective to bind, in a sequence-specific manner to a target sequence of a duplex polynucleotide, at least two different-oriented Watson/Crick • base • -pairs at selected positions in the target sequence. The composition includes an uncharged backbone with 5- or 6-membered cyclic backbone structures and selected • bases • attached to the backbone structures effective to hydrogen bond specifically with different oriented • base • -pairs in the target sequence. Also disclosed are subunits useful for the construction of the polymer composition. The present invention further includes methods for (i) coupling a first free or polymer-terminal subunit, and (ii) isolating, from a liquid sample, a target duplex nucleic acid fragment having a selected sequence of • base • -pairs.

19. 5,405,760, Apr. 11, 1995, Process for producing recombinant McrBC endonuclease and cleavage of methylated DNA; Elisabeth A. Raleigh, et al., 435/91.53, 199, 252.33, 320.1; 536/23.2 [IMAGE AVAILABLE]
US PAT NO: 5,405,760 [IMAGE AVAILABLE] L15: 19 of 191
ABSTRACT:
The present invention relates to a recombinant McrBC endonuclease obtainable from Escherichia coli, two components of which, McrB.sub.L and McrC, have been purified in active form. McrBC is

active in the presence of GTP and at a low pH. The McrBC endonuclease is also substantially free of a third component, McrB.sub.S, which is believed to inhibit or otherwise interfere with the activity of the enzyme. McrBC has various desirable properties, including the ability to recognize a methylated DNA sequence and also its ability to cleave such a sequence in the presence of GTP. Also provided is a process for the production of recombinant McrBC endonuclease, a process for the determination of the modification state of DNA a process for the determination of an epigenetic alteration or defect (including "imprinting"), as well as a process for identifying and isolating additional enzymes that cleave modified DNA.

20. 5,395,928, Mar. 7, 1995, Chromatographic separation of phosphorothioate oligonucleotides; B. John Bergot, 536/25.4, 27.13, 55.3 [IMAGE AVAILABLE]

US PAT NO: 5,395,928 [IMAGE AVAILABLE] L15: 20 of 191

ABSTRACT:

A method is provided for the preparation and/or analysis of synthetic phosphorothioate and -dithioate oligonucleotides. In particular, the method permits separation of fully sulfurized phosphorothioate or -dithioate oligonucleotides from incompletely sulfurized defect species on an anion exchange HPLC columns using concentration gradients of novel "soft • base • " anionic eluents, such as bromide, thiocyanate, and the like.

21. 5,395,767, Mar. 7, 1995, Gene for ataxia-telangiectasia complementation group D (ATDC); John P. Murnane, et al., 435/320.1, 69.1, 240.1; 536/23.1, 24.3 [IMAGE AVAILABLE]

US PAT NO: 5,395,767 [IMAGE AVAILABLE] L15: 21 of 191

ABSTRACT:

Disclosed herein is a new gene, an AT gene for complementation group D, the ATDC gene and fragments thereof. Nucleic acid probes for said gene are provided as well as proteins encoded by said gene, cDNA therefrom, preferably a 3 kilobase (kb) cDNA, and recombinant nucleic acid molecules for expression of said proteins. Further disclosed are methods to detect mutations in said gene, preferably methods employing the polymerase chain reaction (PCR). Also disclosed are methods to detect AT genes from other AT complementation groups.

22. 5,396,023, Jan. 31, 1995, Backbone modified oligonucleotide analogs and preparation thereof through reductive coupling; Yogesh S. Sanghvi, et al., 536/25.3, 23.1, 25.33, 25.34, 25.6 [IMAGE AVAILABLE]

US PAT NO: 5,396,023 [IMAGE AVAILABLE] L15: 22 of 191

ABSTRACT:

Methods for preparing oligonucleotide analogs which have improved nuclease resistance and improved cellular uptake are provided. In preferred embodiments, the methods involve reductive coupling of 3'- and 4'-substituted or 4'- and 3'-substituted nucleosidic synthons.
23. 5,380,835, Jan. 10, 1995, Silyl phosphorylating reagents and methods of using them; Joseph E. Oelebuski, et al., 536/18.5, 25.3, 26.5; 558/199 [IMAGE AVAILABLE]

US PAT NO: 5,380,835 [IMAGE AVAILABLE] L15: 23 of 191
ABSTRACT:
Oligonucleotide phosphorylating reagents wherein the silyl moiety has three bulky substituents, such as phenyl or t-butyl, and the silyl moiety is attached to the carbon of an ethanol group whose hydroxyl is an activated phosphate group. The preferred compound is 2-
triphenylsilylethyl-2-cyanoethyl-N,N
diisopropylaminophosphoramidite. The method of using this reagent to phosphorylate the 5'-OH of nucleosides and oligonucleotides is also disclosed. Nucleosides and nucleotides whose 5'-OH has been phosphorylated by the above reagent are also disclosed. The phosphorylated intermediate bearing the silyl group may be separated from failure product on the basis of bulky substituents on the silyl protecting group, which can be later removed by fluoride ion.
24. 5,376,658, Dec. 27, 1994, 5,10-methylene-tetrahydrofolate as a modulator of a chemotherapeutic agent; Colin P. Spears, et al., 514/274 [IMAGE AVAILABLE]

US PAT NO: 5,376,658 [IMAGE AVAILABLE] L15: 24 of 191
ABSTRACT:
The present invention relates to the compound 5,10-methylene-tetrahydrofolate (CH.sub.2 FH.sub.4), and its solution product isomer FH.sub.4, therapeutic uses of these compounds, and compositions thereof. CH.sub.2 FH.sub.4 and FH.sub.4 strongly modulate the in vivo antitumor effects of 5-Fluorouracil.

25. 5,376,529, Dec. 27, 1994, Lactam-containing compositions and methods useful for the hybridization of nucleic acids; Jeffrey Van Ness, et al., 435/6; 540/451, 463, 485, 526, 527; 546/243; 549/347 [IMAGE AVAILABLE]
US PAT NO: 5,376,529 [IMAGE AVAILABLE] L15: 25 of 191
ABSTRACT:
This invention relates to novel methods for the release of nucleic acids from cells in complex biological samples or specimens to prepare and make available the nucleic acid material present for a hybridization assay or for extraction. Novel methods for hybridization of nucleic acids are also presented. In particular methods are described for isolating nucleic acid from a sample containing a complex biological mixture of nucleic acid and non-nucleic acids wherein the sample is combined with a

hybridization medium comprising a lactam which promotes and enables nucleic acid pairing when complementary nucleic acid is introduced. The lactam is preferably about 5 to about 70% of the hybridization medium and is most preferably 2-pyrrolidone, N-ethyl-2-pyrrolidone, N-cyclohexyl-2- pyrrolidone, N-dodecyl-2-pyrrolidone, N-methyl-2-pyrrolidone, N-hydroxyethyl-2-pyrrolidone, N-methyl-2-piperidone, 2-.epsilon.-caprolactam, N-methyl-2-caprolactam, 2-piperidone or N-(4-hydroxybenzyl)pyrrolidone.

26. 5,374,527, Dec. 20, 1994, High resolution DNA sequencing method using low viscosity medium; Paul D. Grossman, 435/6; 204/180.1, 182.8, 299R; 435/91.1; 436/94; 935/19, 77 [IMAGE AVAILABLE]

US PAT NO: 5,374,527 [IMAGE AVAILABLE] L15: 26 of 191
ABSTRACT:
A DNA sequencing method for use in sequencing a DNA target sequence up to 300 • bases • , preferably up to 500 • bases • or greater in length, by electrophoretically separating a mixture of single-stranded DNA sequencing fragments in a capillary tube. The method employs an aqueous denaturing solution comprising between about 4 and about 7 weight percent linear polyacrylamide molecules having an average molecular weight of between about 20 and about 100 kDa. The low-viscosity of the solution allows rapid loading and reloading of such solution into the capillary tube.

27. 5,369,019, Nov. 29, 1994, Pasteurella vaccine; Niels T. Foged, et al., 435/69.3; 424/190.1, 255.1; 435/69.1, 71.1, 252.33, 320.1; 536/23.4, 23.7 [IMAGE AVAILABLE]

US PAT NO: 5,369,019 [IMAGE AVAILABLE] L15: 27 of 191
ABSTRACT:

A vaccine for immunizing animals against diseases caused by microorganisms producing an osteolytic toxin is disclosed. The vaccine contains a Pasteurella multocida toxin or derivative thereof that has been rendered non-toxic by genetic and/or biochemical means. The toxin or derivative is encoded by a nucleotide sequence from Pasteurella multocida toxin which is inserted in an expression vector capable of replicating in a suitable host microorganism in which the sequence may be expressed.
28. 5,367,060, Nov. 22, 1994, Structure, production and use of heregulin; Richard L. Vandlen, et al., 530/399, 350 [IMAGE AVAILABLE]
US PAT NO: 5,367,060 [IMAGE AVAILABLE] L15: 28 of 191
ABSTRACT:
A novel polypeptide with binding affinity for the p185.sup.HER2 receptor, designated heregulin-.alpha., has been identified and purified from cultured human cells. DNA sequences encoding

additional heregulin polypeptides, designated heregulin-.alpha., heregulin-.beta.1, heregulin-.beta.2, heregulin-.beta.2-like, and heregulin-.beta.3, have been isolated, sequenced and expressed. Provided herein are nucleic acid sequences encoding the amino acid sequences of heregulins useful in the production of heregulins by recombinant means. Further provided are the amino acid sequences of heregulins and purification methods therefor. Heregulins and their antibodies are useful as therapeutic agents and in diagnostic methods.

29. 5,366,887, Nov. 22, 1994, Ri T-DNA promoters; Jerry L. Slightom, et al., 435/240.4, 172.3, 240.1, 320.1; 536/23.1, 24.1; 935/6, 35, 56 [IMAGE AVAILABLE]

US PAT NO: 5,366,887 [IMAGE AVAILABLE] L15: 29 of 191

ABSTRACT:

The sequence of the T.sub.L -DNA of Ri plasmids found in Agrobacterium rhizogenes strains HRI and A4 is disclosed. Sixteen open reading frames bounded by eukaryotic promoters, ribosome binding sites, and polyadenylation sites were found, five of which were observed to be transcripted in a developmentally and phenotypically regulated manner. The use of promoters and polyadenylation sites from pRi T.sub.L -DNA to control expression of heterologous foreign structural genes is taught, using as examples the structural genes for Phaseolus vulgaris storage protein (phaseolin), P. vulgaris lectin, a sweet protein (thaumatin), and Bacillus thuringiensis crystal protein. Vectors useful for manipulation of sequences of the structural genes and T-DNA are also provided.

30. 5,366,874, Nov. 22, 1994, Molecular cloning and expression of biologically-active diphtheria toxin receptor; Leon Eidels, et al., 435/69.1, 7.1, 7.2, 252.3, 320.1; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,366,874 [IMAGE AVAILABLE] L15: 30 of 191

ABSTRACT:

DT-resistant wild-type mouse L-M cells were co-transfected with a cDNA library constructed from RNA of highly toxin-sensitive monkey Vero cells and with a neomycin resistance gene. One DT-sensitive (DT.sup.S) colony was isolated from 8,000 stably-transfected neomycin-resistant L-M colonies screened by replica plate assays. The purified DT.sup.S mouse cells are highly toxin-sensitive (.about.1,000-fold more so than L-M cells and only .about.10-fold less than Vero cells) and are protected from DT toxicity on incubation with a nontoxic competitive DT inhibitor (CRM 197). Importantly, the cell surface receptors on DT.sup.S cells specifically bind radioiodinated DT, which is inhibited by unlabelled DT and the DT receptor-binding domain (HA6DT). A plasmid conferring DT-sensitivity (pDTS) was rescued from DT.sup.S cells, and the screening procedure repeated until a single cDNA encoding the DT receptor was isolated. The cDNA is predicted to encode an integral membrane protein that corresponds to the precursor of a human heparin-binding EGF-like growth

factor. The DT sensitivity protein is thus a growth factor precursor which is exploited by DT, thus allowing the toxin to enter the cell.

31. 5,366,737, Nov. 22, 1994, N-[.omega.,(.omega.-1)-dialkyloxy]- and N-[.omega.,(.omega.-1)-dialkenyloxy]-alk-1-yl-N,N,N,-tetrasubstituted ammonium lipids and uses therefor; Deborah A. Eppstein, et al., 424/450; 264/4.1, 4.33, 4.6; 424/423, 427, 428, 449; 435/829 [IMAGE AVAILABLE]
US PAT NO: 5,366,737 [IMAGE AVAILABLE] L15: 31 of 191
ABSTRACT:
This invention relates to compounds of the formula or an optical isomer thereof wherein R.sup.1 and R.sup.2 are the same or different and are an alkyl or alkenyl group of 6 to 24 carbon atoms; R.sup.3, R.sup.4 and R.sup.5 are the same or different and are alkyl of 1 to 8 carbon atoms, aryl, aralkyl of 7 to 11 carbon atoms, or when two or three of R.sup.3, R.sup.4, and R.sup.5 are taken together to form quinuclidino, piperidino, pyrrolidino, or morpholino; n is 1 to 8; and X is a pharmaceutically acceptable anion.

32. 5,364,934, Nov. 15, 1994, Plasma carboxypeptidase; Dennis T. Drayna, et al., 536/23.2; 435/240.2, 252.3, 320.1 [IMAGE AVAILABLE]
US PAT NO: 5,364,934 [IMAGE AVAILABLE] L15: 32 of 191
ABSTRACT:
A novel polypeptide, designated plasma carboxypeptidase B (PCPB), has been purified from human plasma. It has been cloned from a human liver cDNA library using PCR amplification. Provided herein is nucleic acid encoding PCPB useful in diagnostics and in the recombinant preparation of PCPB. PCPB is used in the preparation and purification of antibodies thereto, in the purification of plasminogen, in the inhibition of plasminogen activation by t-PA in the presence of fibrinogen, and in diagnostic assays.

33. 5,364,790, Nov. 15, 1994, In situ PCR amplification system; John G. Atwood, et al., 435/288; 359/398; 422/99, 102, 104; 435/290, 316, 809 [IMAGE AVAILABLE]

US PAT NO: 5,364,790 [IMAGE AVAILABLE] L15: 33 of 191
ABSTRACT:
A complete in situ PCR system for amplification of nucleic acids contained in a prepared cell or tissue sample. The containment system for the PCR sample comprises a glass microscope slide, a specimen sample containing the target nucleic acid sequence mounted on the slide, a flexible plastic cover over the sample, and a retaining assembly fastened to the slide and to the cover to retain and seal a reaction mixture against the sample during thermal cycling. The retaining assembly includes a rigid ring on a rim portion of the cover, a cross beam having spaced parallel

rails joined by opposite flat ends, and a pair of clips which are pressed over the ends and opposite sides of the slide to fasten the cross beam and cover to the slide.

34. 5,363,697, Nov. 15, 1994, Scanning probe microscope, molecular processing method using the scanning probe microscope and DNA • base • arrangement detecting method; Tohru Nakagawa, 73/105; 250/306 [IMAGE AVAILABLE]

US PAT NO: 5,363,697 [IMAGE AVAILABLE] L15: 34 of 191

ABSTRACT:
This invention relates to a scanning probe microscope which examines or processes directly the structure of substance surfaces at the molecular or atomic level, and a method for processing molecules using a scanning probe microscope and a method for detecting DNA • base • arrangement. A scanning probe microscope has a probe approaching or contacting the substance surface to detect a physical quantity between the substance surface and the probe, wherein the physical quantity is what is interacted or chemically reacted between the substance surface and the molecules or atom groups which act as a sensor and are fixed on the probe, scanning at an atomic level of precision. Therefore, surface structure within a microscopic region can be examined or processed at the molecular or atomic level. A method for detecting DNA • base • arrangement with any one of three or four kinds of probes fixed with any one of four different kinds of molecules interacting four kinds of • bases • consisting of DNA, by approaching single stranded DNA fixed on a substrate, measuring the force and scanning by an atomic force microscope at an atomic level of precision.

35. 5,362,623, Nov. 8, 1994, Sequence specific DNA binding by p53; Bert Vogelstein, et al., 435/6, 320.1; 536/24.1, 24.31 [IMAGE AVAILABLE]

US PAT NO: 5,362,623 [IMAGE AVAILABLE] L15: 35 of 191

ABSTRACT:
Specific sequences in the human genome are the sites of strong binding of wild-type p53 protein, but not mutant forms of the protein. These sequences are used diagnostically to detect cells in which the amount of wild-type p53 is diminished. The sequences can also be used to screen for agents which correct for loss of wild-type p53 to DNA in cancer cells.

36. 5,360,714, Nov. 1, 1994, Hepadnavirus polymerase gene product having RNA-dependent DNA priming and reverse transcriptase activities and methods of measuring the activities thereof; Christoph Seeger, 435/5; 252/193.11; 435/15, 69.1, 91.51; 536/23.2, 23.72; 935/14, 17 [IMAGE AVAILABLE]

US PAT NO: 5,360,714 [IMAGE AVAILABLE] L15: 36 of 191

ABSTRACT:
An enzymatically active composition of matter, comprising an

extracellular combination of a substantially virus-free hepadnavirus polymerase gene product and an RNA template for hepadnavirus minus strand DNA synthesis, is provided. The composition possesses a DNA priming activity and a reverse transcriptase activity. The hepadnavirus polymerase gene product is produced by in vitro expression of a hepadnavirus pol gene. The enzymatically active composition of matter is used in rapid in vitro assays to screen potential anti-hepadnaviral agents. Assays for various functions of the hepadnavirus DNA polymerase are provided, including: (1) binding of the polymerase gene product to hepadnavirus pre-genomic RNA; (2) DNA priming activity of the polymerase gene product; and (3) reverse transcriptase activity of the polymerase gene product.

37. 5,359,047, Oct. 25, 1994, Nucleic acids encoding DNA structure-specific recognition protein and uses therefor; Brian A. Donahue, et al., 536/23.5; 435/6; 530/350; 536/23.1; 935/3, 9, 78 [IMAGE AVAILABLE]

US PAT NO: 5,359,047 [IMAGE AVAILABLE] L15: 37 of 191

ABSTRACT:

DNA structure specific recognition protein of eukaryotic origin and DNA encoding such a factor, as well as probes specific for DNA structure specific recognition protein or DNA encoding it and methods of detecting DNA structure specific recognition protein in eukaryotic cells. In particular, a mammalian cellular factor that selectively recognizes and binds DNA damaged or modified by a drug (the anticancer drug, cis-diamminedichloroplatinum (II) or cisplatin) has been identified.

38. 5,354,657, Oct. 11, 1994, Process for the highly specific detection of nucleic acids in solid; Hans J. Holtke, et al., 435/6; 536/24.3; 935/77, 78 [IMAGE AVAILABLE]

US PAT NO: 5,354,657 [IMAGE AVAILABLE] L15: 38 of 191

ABSTRACT:

The present invention provides a process for the detection of nucleic acids of definite sequence by hybridisation with two single-stranded nucleic acid probes present in the same solution phase complementary to different regions of the nucleic acid to be detected, one nucleic acid probe serving as detector probe and containing as labelling at least one hapten bound via a chemical linkage and the other nucleic acid probe serving as capturing probe and being bound to a solid matrix, wherein, as hapten, a steroid is used which on at least one position of the detector probe, which does not participate in the hydrogen bridge formation with the nucleic acid to be detected, is • covalently • bound via a bridge of at least four atoms, the nucleic acid to be detected, present in solution, is incubated with the detector probe and the capturing probe in any desired sequence, whereby the binding of the capturing probe on the matrix with the nucleic acid to be detected is brought about before, during or after the incubation, the remaining solution is separated off from the

matrix-bound complex of the capturing probe, nucleic acid to be detected and detector probe and the complex detected via an anti-hapten antibody which is labelled.

39. 5,348,853, Sep. 20, 1994, Method for reducing non-specific priming in DNA amplification; Chang-Ning J. Wang, et al., 435/6, 91.2 [IMAGE AVAILABLE]

US PAT NO: 5,348,853 [IMAGE AVAILABLE] L15: 39 of 191
ABSTRACT:
This invention relates to a homogeneous process for amplifying a target sequence in a nucleic acid sample and detecting amplification in the absence of a separation step. The invention further provides a method for nucleic acid amplification under conditions which substantially reduce the occurrence of nonspecific amplification. Products and an apparatus related to the homogeneous process are also described.

40. 5,346,991, Sep. 13, 1994, Tissue factor mutants useful for the treatment of myocardial infarction and coagulopathic disorders; Soumitra Roy, et al., 530/350; 435/172.3; 530/381, 809 [IMAGE AVAILABLE]
US PAT NO: 5,346,991 [IMAGE AVAILABLE] L15: 40 of 191
ABSTRACT:
A tissue factor protein mutant capable of neutralizing the ability of endogenous tissue factor to induce coagulation is provided. A representative tissue factor mutant designated K165A, K166A TF is useful in a method for inhibiting thrombin-induced platelet aggregation in a mammal, either separately or in combination with a thrombolytic agent, an anticoagulant, or a GPII.sub.b III.sub.a inhibitor.

41. 5,340,716, Aug. 23, 1994, Assay method utilizing photoactivated chemiluminescent label; Edwin F. Ullman, et al., 435/6, 7.7 [IMAGE AVAILABLE]

US PAT NO: 5,340,716 [IMAGE AVAILABLE] L15: 41 of 191
ABSTRACT:

Methods are disclosed for determining an analyte in a medium suspected of containing the analyte. One method comprises providing (1) a medium suspected of containing the analyte, (2) a label reagent comprising a first specific binding pair (sbp) member associated with a photochemically activatable chemiluminescent compound wherein the first sbp member is capable of binding to the analyte or to a second sbp member to form a complex related to the presence of the analyte. The method further comprises photochemically activating the chemiluminescent compound. The amount of luminescence generated by the chemiluminescent compound is detected. The amount thereof is related to the amount of analyte in the medium. Compositions and

kits are also disclosed.
42. 5,334,711, Aug. 2, 1994, Synthetic catalytic oligonucleotide structures; Brian Sproat, et al., 536/24.5; 424/94.1; 435/183; 514/44; 536/23.1, 24.3, 25.3; 935/3 [IMAGE AVAILABLE]

US PAT NO: 5,334,711 [IMAGE AVAILABLE] L15: 42 of 191
ABSTRACT:
A synthetic catalytic oligonucleotide structure and nucleotides having the general structural formula (I) contains: ##STR1## in which B represents a nucleoside • base • which is in particular selected from the group comprising adenin-9-yl (A), cytosin-1-yl (C), guanin-9-yl (G), uracil-1-yl (U), uracil-5-yl (.psi.), hypoxanthin-9-yl (I), thymin-1-yl (T) and 2-aminoadenin-9-yl, V in each nucleotide is independently an O or a CH.sub.2 group, X and W can in each nucleotide be the same or different and are independently of each other O, S, NH.sub.2, alkyl or alkoxy groups with 1 to 10, preferably with 1 to 4 carbon atoms, R is hydrogen or a straight-chained or branched alkyl, alkenyl or alkinyl group with 1 to 10 carbon atoms which is substituted, if desired, with halogen, cyano, isocyano, nitro, amino, carboxyl, hydroxyl or/and mercapto groups, and in which in at least one of the nucleotides the residue R in formula (I) is different from hydrogen and is suitable for the cleavage of a nucleic acid target sequence.
43. 5,332,666, Jul. 26, 1994, Method, system and reagents for DNA sequencing; James M. Prober, et al., 435/91.5, 6, 968; 436/56, 805; 935/77 [IMAGE AVAILABLE]

US PAT NO: 5,332,666 [IMAGE AVAILABLE] L15: 43 of 191
ABSTRACT:
A DNA sequencing system and method are described to detect the presence of radiant energy emitted from different excited reporter dye-labeled species (DNA fragments) following separation in time and/or space, and the identity of the species which emit radiant energy closely spaced in wavelength. Functions of the emitted energy are obtained which vary over the wavelengths of the closely spaced spectra in different senses and the functions ratioed, whereby the ratio is indicative of the identity of the DNA fragments. The emitting portion of the reporter-labeled DNA fragment is preferably one of a family of fluorescent dyes based on 9-carboxyethyl-6-hydroxy-3-oxo-3H-xanthene. These xanthene dyes are • covalently • attached to the DNA fragments through the carboxylic acid functionality, preferably via an amide linkage. The dyes may be protected by including an alkoxy group at the 9-position. A spacer may be inserted between the dye and the amine. The fluorescent dye preferably is attached to the DNA chain terminators and provides many advantages. Thus only DNA sequencing fragments resulting from bona fide termination events will carry a reporter. The DNA sequencing may also be labeled using the xanthene dyes which have general utility as fluorescent labels. Also acyclonucleoside triphosphates are described as being useful as chain terminators in DNA sequencing using a

modification of the Sanger method.
44. 5,328,824, Jul. 12, 1994, Methods of using labeled nucleotides; David C. Ward, et al., 435/6, 7.1, 91.2; 536/22.1, 25.3, 25.32; 935/78 [IMAGE AVAILABLE]

US PAT NO: 5,328,824 [IMAGE AVAILABLE] L18: 44 of 191
ABSTRACT:
Compounds having the structure: ##STR1## wherein B represents a purine, 7-deazapurine, or pyrimidine moiety ▼ covalently ▼ bonded to the C.sup.1' -position of the sugar moiety, provided that when B is purine or 7-deazapurine, it is attached at the N.sup.9 -position of the purine or 7-deazapurine and when B is pyrimidine, it is attached at the N.sup.1 -position;
wherein A represents a moiety consisting of at least three carbon atoms which is capable of forming a detectable complex with a polypeptide when the compound is incorporated into a double-stranded ribonucleic acid, deoxyribonucleic acid duplex, or DNA-RNA hybrid;
wherein the dotted line represents a chemical linkage joining B and A, provided that if B is purine, the linkage is attached to the 8-position of the purine, if B is 7-deazapurine, the linkage is attached to the 7-position of the deazapurine, and if B is pyrimidine, the linkage is attached to the 5-position of the pyrimidine; and
wherein each of x, y and z represents ##STR2## either directly, or when incorporated into oligo- and polynucleotides, provide probes which are widely useful.
Applications include detection and localization of polynucleotide sequences in chromosomes, fixed cells, tissue sections, and cell extracts. Specific applications include chromosomal karyotyping, clinical diagnosis of nucleic acid-containing etiological agents, e.g. bacteria, viruses, or fungi, and diagnosis of genetic disorders.

45. 5,324,483, Jun. 28, 1994, Apparatus for multiple simultaneous synthesis; Donna R. Cody, et al., 422/131, 99, 101, 104 [IMAGE AVAILABLE]
US PAT NO: 5,324,483 [IMAGE AVAILABLE] L18: 45 of 191
ABSTRACT:
An apparatus and method which provides a suitable location for multiple, simultaneous synthesis of compounds. The apparatus consists of: a reservoir block having a plurality of wells; a plurality of reaction tubes, usually gas dispersion tubes, having filters on their lower ends; a holder block, having a plurality of apertures; and a manifold, which may have ports to allow introduction/maintenance of a controlled environment. The manifold top wall has apertures and a detachable plate with identical apertures. The apparatus is constructed from materials which will accommodate heating, cooling, agitation, or corrosive reagents. Gaskets are placed between the components. Rods or clamps are provided for fastening the components together. Apparatus operation involves placing the filters on the lower

ends of the reaction tubes in the reservoir block wells, and the upper ends passing through the holder block apertures and into the manifold. The apparatus provides in excess of 1 mg of each product with structural knowledge and control over each compound. Using the apparatus a series of building blocks are • covalently • attached to a solid support. These building blocks are then modified by • covalently • adding additional different building blocks or chemically modifying some existing functionality until the penultimate structure is achieved. This is then cleaved from the solid support by another chemical reaction into the solution within the well yielding an array of newly synthesized individual compounds, which after postreaction modification, if necessary, are suitable for testing for activity.

46. 5,317,009, May 31, 1994, Anti-HIV proteins GAP 31, DAP 30 and DAP 32 and therapeutic uses thereof; Sylvia Lee-Huang, et al., 514/8, 12, 885; 530/370, 377, 387.1, 395 [IMAGE AVAILABLE]

US PAT NO: 5,317,009 [IMAGE AVAILABLE] L15: 46 of 191

ABSTRACT:
New proteins, termed GAP 31, obtainable from the seeds of Gelonium multiflorum, and DAP 30 and DAP 32, obtainable from the leaves or seeds of Dianthus caryophyllus, or the above proteins produced by recombinant means, are useful for treating HIV infections. In treating HIV infections, the protein is administered alone or in conjunction with other anti-HIV therapeutics. Also provided are processes for purifying the proteins, DNA sequences encoding the proteins, hosts expressing the proteins, recombinant DNA methods for expressing the proteins, and antibodies specific for the proteins.

47. 5,312,527, May 17, 1994, Voltammetric sequence-selective sensor for target polynucleotide sequences; Susan R. Mikkelsen, et al., 204/153.12, 403, 412; 435/288, 291, 810, 917; 436/94, 501 [IMAGE AVAILABLE]

US PAT NO: 5,312,527 [IMAGE AVAILABLE] L15: 47 of 191

ABSTRACT:
The present invention relates to a voltammetric sequence-selective sensor for target polynucleotide sequences which essentially comprises: an immobilized polynucleotide probe having one end • covalently • bound onto an amperometric electrode. The immobilized probe includes a target binding region capable of hybridizing to the target polynucleotide sequences forming an immobilized heteroduplex having at least a hybridized region. The sequence-selective sensor of the present invention also comprises means for voltammetrically detecting immobilized heteroduplexes. There is also provided a method for detecting the presence of a target polynucleotide analyte in a physiological sample, which comprises the steps of incubating the prepared physiological sample with the voltammetric sequence-selective sensor of the present invention; voltammetrically detecting immobilized heteroduplexes; and comparing the resulting

voltammogram with a control voltammogram.

48. 5,304,603, Apr. 19, 1994, Leydig cell stimulator; C. Yan Cheng, et al., 514/12, 15, 21; 530/397, 398, 399, 416, 417; 935/60 [IMAGE AVAILABLE]

US PAT NO: 5,304,603 [IMAGE AVAILABLE] L15: 48 of 191
ABSTRACT:
The present invention relates to a compound which when administered to Leydig cells in the testes stimulates the production of androgen such as testosterone. This compound, when mixed with other known compounds, can produce testosterone levels in excess of those obtained by the administration of a maximal stimulatory dose of Lutenizing Hormone (LH).

49. 5,292,873, Mar. 8, 1994, Nucleic acids labeled with naphthoquinone probe; Steven E. Rokita, et al., 536/24.3, 32; 548/547, 548 [IMAGE AVAILABLE]

US PAT NO: 5,292,873 [IMAGE AVAILABLE] L15: 49 of 191
ABSTRACT:
A sequence directed reagent is constructed by conjugating a methyl naphthoquinone derivative to a hexamethylamino linker attached to the 5' terminus of an oligonucleotide. Annealing this modified fragment of DNA to its complementary sequence allows for target modification subsequent to photochemical activation. The product of this reaction is a • covalent • crosslink between the reagent and target strands resulting from an alkylation of DNA by the photoexcited quinone. The modified sequence is not labile to acid, • base • or reductants, and blocks the exonuclease activity of the Klenow fragment of DNA polymerase I. In another embodiment, a highly reactive moiety, such as Br is attached to the methyl group of the naphthoquinone derivative. This reagent is similarly linked to an oligonucleotide probe. Activation of this probe linked alkylating agent is by a reductive signal which may either naturally occur within the cell, such as an enzyme, or introduced into the media containing the target molecule.

50. 5,292,653, Mar. 8, 1994, Equine herpesvirus 1 tk mutants; Malon Kit, et al., 435/235.1, 172.3, 320.1; 935/32 [IMAGE AVAILABLE]

US PAT NO: 5,292,653 [IMAGE AVAILABLE] L15: 50 of 191
ABSTRACT:
The present invention relates to Equine Herpesvirus Type 1 mutants which fail to produce any functional thymidine kinase as a result of a deletion and/or insertion in the EHV-1 thymidine kinase gene.

51. 5,286,654, Feb. 15, 1994, Detection and purification of activin polypeptide; Edward T. Dow, et al., 436/501, 536;

530/389.22, 395, 413 [IMAGE AVAILABLE]

US PAT NO: 5,286,654 [IMAGE AVAILABLE] L15: 51 of 191

ABSTRACT:
An isolated TGF-.beta. supergene family (TSF) receptor polypeptide is provided. This polypeptide preferably is an inhibin/activin receptor polypeptide and has at least 75% sequence identity with the mature human inhibin/activin receptor sequence. Also provided is a method for purifying TGF-.beta. supergene family members such as inhibin or activin using the polypeptide, and a method for screening for compounds with TGF-.beta. supergene family member activity by contacting the compound with the polypeptide and detecting if binding has occurred and the compound is active.

US. 5,279,954, Jan. 18, 1994, Exopeptidase catalyzed site-specific bonding of supports, labels and bioactive agents to proteins; Fred W. Wagner, et al., 435/176, 177, 180, 181; 436/524, 528, 531, 532; 530/811, 812, 815, 816 [IMAGE AVAILABLE]

US PAT NO: 5,279,954 [IMAGE AVAILABLE] L15: 52 of 191

ABSTRACT:
The invention provides a means for attaching a label, support or bioactive agent to a protein with an exopeptidase at a site that is remote from the active site of the protein. More specifically the invention is directed to a method for the attachment of an amino acid, amine and alcohol nucleophile to the carbonyl terminus of a protein. In one embodiment, a labeled nucleophile is attached to a protein such as an antibody. In other embodiments, the invention is directed to a method for the attachment of a protein to an immobilization support and to a method for the attachment of a bioactive agent to a protein.

US. 5,276,013, Jan. 4, 1994, Conjugates of biologically stable polyfunctional molecules and polynucleotides for treating systemic lupus erythematosus; Michael J. Conrad, et al., 514/2; 424/78.02, 78.24, 78.31; 514/44, 885; 536/24.2 [IMAGE AVAILABLE]

US PAT NO: 5,276,013 [IMAGE AVAILABLE] L15: 53 of 191

ABSTRACT:
Chemically defined conjugates of biologically stable valency platform molecules, such as copolymers of D-glutamic acid and D-lysine or polyethylene glycol, and polynucleotide duplexes of at least 20 • base • pairs that have significant binding activity for human lupus anti-dsDNA autoantibodies. The duplexes are preferably homogeneous in length structure and are bound to the valency platform molecule via reaction between a functional group located at or proximate a terminus of each duplex and functional groups on the valency platform molecule. These conjugates are tolerogens for human systemic lupus erythematosus.

54. 5,270,163, Dec. 14, 1993, Methods for identifying nucleic acid ligands; Larry Gold, et al., 435/6, 91.2 [IMAGE AVAILABLE]
US PAT NO: 5,270,163 [IMAGE AVAILABLE] L15: 54 of 191
ABSTRACT:
The SELEX (Systematic Evolution of Ligands by EXponential Enrichment) method is disclosed for the identification of nucleic acid ligands. A candidate mixture of single stranded nucleic acids having regions of randomized sequence is contacted with a target compound and those nucleic acids having an increased affinity to the target are partitioned from the remainder of the candidate mixture. The partitioned nucleic acids are amplified to yield a ligand enriched mixture.

55. 5,270,030, Dec. 14, 1993, Fibrin binding domain polypeptide and method of producing; Tikva Vogel, et al., 424/1.69, 9.341, 9.4; 435/69.1, 240.1, 252.3, 252.33, 320.1; 530/350, 395 [IMAGE AVAILABLE]
US PAT NO: 5,270,030 [IMAGE AVAILABLE] L15: 55 of 191
ABSTRACT:
This invention provides an imaging agent which comprises a polypeptide labeled with an imageable marker, such polypeptide having an amino acid sequence substantially present in the fibrin binding domain of naturally-occurring human fibronectin and being capable of binding to fibrin. The invention further provides a method wherein the imaging agent is used for imaging a fibrin-containing substance, i.e., a thrombus or atherosclerotic plaque. Further provided are plasmids for expression of polypeptides having an amino acid sequence substantially present in the fibrin binding domain of naturally-occurring human fibronectin and being capable of binding to fibrin, hosts containing these plasmids, methods of producing the polypeptides, methods of treatment using the polypeptides, and methods of recovering, refolding and reoxidizing the polypeptides. The invention also provides for purified polypeptides substantially free of other substances of human origin which have an amino acid sequence substantially present in the fibrin binding domain of naturally-occurring human fibronectin and which are capable of binding to fibrin.
56. 5,266,459, Nov. 30, 1993, Gaucher's disease: detection of a new mutation in intron 2 of the glucocerebrosidase gene; Ernest Beutler, 435/6, 91.2; 536/23.1; 935/77, 78 [IMAGE AVAILABLE]

US PAT NO: 5,266,459 [IMAGE AVAILABLE] L15: 56 of 191
ABSTRACT:
A method for detecting a new Gaucher disease mutation in an allele in a human having a point mutation of an adenine nucleotide substituted for a guanine nucleotide at nucleotide position 1 in the normal
glucocerebrosidase gene intron 2 is provided. Identification of the mutation is accomplished by first amplifying, with a polymerase chain reaction (PCR) primer, a region of human genomic

DNA containing nucleotide position 1 of glucocerebrosidase gene intron 2 followed by detection of the mutation.

57. 5,262,536, Nov. 16, 1993, Reagents for the preparation of 5'-tagged oligonucleotides; Frank W. Hobbs, Jr., 546/25; 536/25.32; 549/223, 283; 558/168, 191, 192, 218 [IMAGE AVAILABLE]

US PAT NO: 5,262,536 [IMAGE AVAILABLE] L18: 57 of 191

ABSTRACT:

Fluorescent reagents possessing an activated phosphate for the convenient • covalent • coupling to the 5'-hydroxyl of oligonucleotides. A class of 5'-fluorescence-tagged oligonucleptides is also disclosed.

58. 5,262,177, Nov. 16, 1993, Recombinant viruses encoding the human melanoma-associated antigen; Joseph P. Brown, et al., 435/235.1; 424 185.1, 199.1, 232.1; 435/69.3, 172.3, 240.2, 252.3, 252.33, 320.1; 530/350; 536/23.5; 935/9, 32, 41, 57, 65, 70, 73 [IMAGE AVAILABLE]

US PAT NO: 5,262,177 [IMAGE AVAILABLE] L18: 58 of 191

ABSTRACT:

Peptides or proteins related to a melanoma associated antigen are described. These are produced in large quantities via recombinant DNA techniques and/or by chemical synthetic methods. The peptides or proteins can be used as immunogens in vaccine formulations which can induce an immune response that selectively destroys melanoma cells in a vaccinated individual. Where the peptides or proteins are expressed by a recombinant virus, inactivated or live virus vaccine formulations may be prepared.

59. 5,260,433, Nov. 9, 1993, Saccharide specific binding system labeled nucleotides; Dean Engelhardt, et al., 536/23.1; 435/6; 536/24.3, 25.32 [IMAGE AVAILABLE]

US PAT NO: 5,260,433 [IMAGE AVAILABLE] L18: 59 of 191

ABSTRACT:

The present invention provides nucleotides and polynucleotides which are chemically modified or labeled so as to be capable of ready detection when attached to and/or incorporated in nucleic acid material. More particularly, this invention provides a nucleotide selected from the group consisting of (i) a ribonucleotide having the formula, ##STR1## wherein PM is a phosphate moiety, SM is a sugar moiety, • BASE • is a pyrimidine, purine or 7-deazapurine moiety, and Sig is a saccharide moiety. PM is attached at the 2',3' or 5' position of SM, • BASE • is attached to the 1' position of SM from the N.sup.1 position when • BASE • is a pyrimidine or • covalently • attached to SM; and (ii) a nucleotide having the formula, ##STR2## wherein PM, SM, • BASE • and Sig are as defined above but PM is attached to the 3' or the 5' position of SM when said nucleotide is a deoxyribonucleotide and at the 2', 3' or 5' position when said nucleotide is a ribonuclectide, • BASE • is attached to the 1' position of SM from the N.sup.1 position when

▼ BASE ▼ is a pyrimidine or the N.sup.9 position when ▼ BASE ▼ is a purine, and wherein Sig is ▼ covalently ▼ attached to PM.

60. 5,258,302, Nov. 2, 1993, DNA for expression of aprotinin in methylotrophic yeast cells; Thomas S. Vedvick, et al., 435/254.23, 320.1; 530/300; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,258,302 [IMAGE AVAILABLE] L15: 60 of 191
ABSTRACT:

Biologically active aprotinin (APR) molecules, naturally occurring, relatively short, single chain polypeptides, are prepared by growing methylotrophic yeast transformants containing in their genome at least one copy of a DNA sequence operably encoding APR, in operational association with a DNA sequence encoding the S. cerevisiae alpha mating factor pre-pro sequence (including a processing sequence selected from lys-arg-(glu-ala).sub.n, wherein n is an integer falling in the range of 0-3), both under the regulation of a promoter region of a gene of a methylotrophic yeast, under conditions allowing expression of said DNA sequences, and secretion of APR molecules into the culture medium. Also disclosed are novel DNA fragments and novel recombinant yeast strains which are useful in the practice of the present invention.

61. 5,256,642, Oct. 26, 1993, Compositions of soluble complement receptor 1 (CR1) and a thrombolytic agent, and the methods of use thereof; Douglas T. Fearon, et al., 514/8; 424/94.63, 94.64; 435/215, 216; 514/2; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,256,642 [IMAGE AVAILABLE] L15: 61 of 191
ABSTRACT:
The present invention relates to compositions comprising soluble complement receptor 1 (CR1) and a thrombolytic agent. In a specific embodiment, the thrombolytic agent is anisoylated human plasminogen-streptokinase activator complex (ASPAC). The invention further relates to methods for treating thrombotic conditions in humans and animals by administering a composition comprising soluble CR1 and a thrombolytic agent. In particular, the compositions and methods are useful both for reducing reperfusion injury and ameliorating the other effects of myocardial infarction.

62. 5,252,724, Oct. 12, 1993, Method of extracting particular nucleic acid fragment; Toshihiko Kishimoto, et al., 536/25.4; 435/6, 91.52, 91.53; 935/19 [IMAGE AVAILABLE]

US PAT NO: 5,252,724 [IMAGE AVAILABLE] L15: 62 of 191
ABSTRACT:
A method of extracting a particular nucleic acid fragment containing a nucleic acid sequence of interest from a nucleic acid or nucleic acids mixture, comprising the steps of:

(1) digesting the nucleic acid or nucleic acids mixture with restriction enzymes to obtain a mixture of nucleic acid fragments, said restriction enzymes consisting of (A) two different enzymes capable of producing the particular nucleic acid fragment bearing predetermined and distinct restriction ends on its 5' and 3' terminals and (B) one or more restriction enzymes different from (A), for which the particular nucleic acid fragment contains no relevant restriction sites;
(2) preparing two distinct DNA linkers capable of binding to the respective restriction ends of the particular nucleic acid fragment; (3) allowing the linkers to react with the mixture of nucleic acid fragments;
(4) subjecting the resulting reaction mixture to the first hybridization with an immobilized probe complementary to one of the linkers; (5) isolating the hybridized nucleic acid fragment from the probe; (6) subjecting the isolated nucleic acid fragment to the second hybridization with an immobilized probe complementary to the other linker; and
(7) isolating the hybridized nucleic acid fragment from the probe.

63. 5,242,794, Sep. 7, 1993, Detection of specific sequences in nucleic acids; Norman M. Whiteley, et al., 435/6, 303; 536/25.4; 935/78 [IMAGE AVAILABLE]

US PAT NO: 5,242,794 [IMAGE AVAILABLE] L15: 63 of 191

ABSTRACT:

The invention provides a method for diagnosis of genetic abnormalities or other genetic conditions which can be readily automated. The method is used to determine the presence or absence of a target sequence in a sample of denatured nucleic acid and entails hybridizing the sample with a probe complementary to a diagnostic portion of the target sequence (the diagnostic probe), and with a probe complementary to a nucleotide sequence contiguous with the diagnostic portion (the contiguous probe), under conditions wherein the diagnostic probe remains bound substantially only to the sample nucleic acid containing the target sequence. The diagnostic probe and contiguous probe are then • covalently • attached to yield a target probe which is complementary to the target sequence, and the probes which are not attached are removed. In the preferred mode, one of the probes is labeled so that the presence or absence of the target sequence can then be tested by melting the sample nucleic acid-target probe duplex, eluting the dissociated target probe, and testing for the label. In another embodiment, the testing is accomplished without first removing probes not • covalently • attached, by attaching a hook to the probe that is not labeled, so that the labeled target probe may be recovered by catching the hook. In both instances, the presence of both the diagnostic probe and the contiguous probe is required for the label to appear in the assay. The above method is then applied to the detection of genetic diseases.

64. 5,241,060, Aug. 31, 1993, • Base • moiety-labeled

detectable nucleatide; Dean Engelhardt, et al., 536/25.32, 23.1, 25.6, 26.6 [IMAGE AVAILABLE]

US PAT NO: 5,241,060 [IMAGE AVAILABLE] L15: 64 of 191
ABSTRACT:
The present invention provides nucleotides and polynucleotides which are chemically modified or labeled so as to be capable of ready detection when attached to and/or incorporated in nucleic acid material. More particularly, this invention provides a nucleotide having the formula
PM-SM- ▼ BASE ▼ -Sig
wherein PM is a phosphate moiety, SM is a sugar moiety and ▼ BASE ▼ is a pyrimidine, purine or 7-deazapurine moiety. PM is attached at the 3' or the 5' position of SM when the nucleotide is a deoxyribonucleotide and at the 2', 3' or 5' position when the nucleotide is a ribonucleotide. ▼ BASE ▼ is attached to the 1' position of SM from the N.sup.1 position when ▼ BASE ▼ is a pyrimidine or the N.sup.9 position when ▼ BASE ▼ is a purine or a 7-deazapurine. Sig is a detectable moiety that is ▼ covalently ▼ attached to ▼ BASE ▼ at a position other than the C.sup.5 position when ▼ BASE ▼ is a pyrimidine, at a position other than the C.sup.8 position when ▼ BASE ▼ is a purine and at a position other than the C.sup.7 position when ▼ BASE ▼ is a 7-deazapurine.

65. 5,234,820, Aug. 10, 1993, Exopeptidase catalyzed site-specific bonding of supports, labels and bioactive agents to proteins; Fred W. Wagner, et al., 435/41, 7.1, 7.92, 181; 436/532, 544; 530/816 [IMAGE AVAILABLE]

US PAT NO: 5,234,820 [IMAGE AVAILABLE] L15: 65 of 191
ABSTRACT:
An auxiliary substance such as a label, support, or bioactive agent is attached to a protein at a site that is remote from the active site of the protein by the use of exopeptidase and a nucleophile which is an amino acid, amino acid derivative, amine or alcohol. In one embodiment, the nucleophile is attached to the carboxy terminus of a protein by catalysis with exopeptidase to form an adduct and then the adduct or its combination with a linker arm is bound to the auxiliary substance. In another embodiment, the auxiliary substance or its combination with a linker arm is bound to the nucleophile to form an intermediate substance which is then coupled by catalysis with exopeptidase to the carboxy terminus of a protein.

66. 5,234,811, Aug. 10, 1993, Assay for a new gaucher disease mutation; Ernest Beutler, et al., 435/6, 91.2; 536/23.1; 935/77, 78 [IMAGE AVAILABLE]

US PAT NO: 5,234,811 [IMAGE AVAILABLE] L15: 66 of 191
ABSTRACT:

A method for detecting a new Gaucher disease mutation in an allele in a human having an insertion mutation of a guanine nucleotide adjacent to nucleotide position 57 in the normal glucocerebrosidase gene exon 2 is provided. Identification of the mutation is accomplished by first amplifying, with a polymerase chain reaction (PCR) primer, a region of human genomic DNA containing nucleotide positions 57 and 58 of glucocerebrosidase gene exon 2 followed by detection of the mutation.
67. 5,225,337, Jul. 6, 1993, Ribozyme compositions and methods for use; Hugh D. Robertson, et al., 435/91.31, 5, 6; 536/23.1; 935/77, 78 [IMAGE AVAILABLE]

US PAT NO: 5,225,337 [IMAGE AVAILABLE] L15: 67 of 191
ABSTRACT:
Ribozymes, sequences cleaving RNA, derived from sequences present in the hepatitis delta virus, have been engineered for greater specificity without increasing size. The specific ribozyme sequences are useful as reagents for cleaving RNA for experimental studies as well as antiviral therapies. Examples demonstrating the targeting of these sequences against HIV and Crohn's disease are described in detail. The sequences are also useful as diagnostics for the detection of hepatitis delta virus in tissue and fluid samples, as in blood banking, as well as in isolation and characterization of new viroids having ribozyme activity, using an RNA-specific hybridization method. Based on analysis of the two domain structure of the hepatitis delta virus, it is possible to construct a vector for expression of non-hepatitis delta virus proteins in mammalian cells.

68. 5,223,408, Jun. 29, 1993, Method for making variant secreted proteins with altered properties; David V. Goeddel, et al., 435/69.3, 69.4, 69.52, 69.6, 69.7, 172.3, 189, 195, 215, 216, 226 [IMAGE AVAILABLE]
US PAT NO: 5,223,408 [IMAGE AVAILABLE] L15: 68 of 191
ABSTRACT:
A screening method for the selection of mutagenized proteins that are normally secreted by cells is described. The method includes the development of a cloning vector for the expression of secretory proteins as fusion proteins on the cell surface of transfected mammalian cells. The secreted protein is displayed on the cell surface by fusion with the glycophospholipid membrane anchor of decay accelerating factor (DAF). Tissue-type plasminogen activator (t-PA), which is normally secreted, is used as a model protein. PCR mutagenesis is used to generate random mutations within the Kringle 1 (K1) domain of t-PA. Fluorescence activated cell sorting (FACS) is employed to screen for t-PA mutants possessing a loss of an epitope to a specific Mab, whose nonlinear binding domains overlap with the t-PA clearance receptor contact regions novel t-PA mutants designated N117S, N144S, and K159R were discovered by this method.

69. 5,218,102, Jun. 8, 1993, Nucleic acid probe containing a

terminal carbamyl linking non-radioactive labeling and preparating processes; Alfredo Cravador, et al., 536/24.3; 435/6, 91.5, 188, 810; 436/501; 536/25.31, 25.32, 25.33, 26.12, 26.6, 26.71, 26.72, 26.8; 935/78, 88 [IMAGE AVAILABLE]

US PAT NO: 5,218,102 [IMAGE AVAILABLE] L15: 69 of 191
ABSTRACT:
The subject of the present invention is a nucleic acid probe containing a nucleic acid sequence, wherein the said sequence is linked at its 5' end, via a divalent bifunctional chemical "arm" L, to a "labeling component" M, M being a synthetic or natural molecule which is directly or indirectly detectable in a non-isotopic manner, according to the formula I: ##STR1## in which J=H or OH
n denotes the number of nucleotides from 1 to 100,000
B is a purine or pyrimidine nucleic acid • base • , which varies according to the nucleotide, as appropriate.
The subject of the invention is also a process for preparing such probes, employing an intermediate compound consisting of a nucleotide synthon of formula IV ##STR2## in which J, B, L and R.sub.1 have the meanings given above, B optionally being protected,
R.sub.2 denotes H or any phosphorylated group, optionally protected, suited to the introduction of the compound of formula IV at the 5' end of another nucleotide, for a given type of internucleotide-assembling synthesis.

70. 5,217,866, Jun. 8, 1993, Polynucleotide assay reagent and method; James Summerton, et al., 435/6; 436/501; 935/77, 78 [IMAGE AVAILABLE]
US PAT NO: 5,217,866 [IMAGE AVAILABLE] L15: 70 of 191
ABSTRACT:

A diagnostic reagent and system for determination of a single-stranded polynucleotide analyte having a selected target sequence. The reagent includes a solid support and multiple support-bound polymers designed to bind specifically to the analyte. Each polymer is composed of a sequence of • base • -complementary recognition moieties which can bind specifically to corresponding contiguous • bases • in the analyte target sequence, and an unbranched, substantially uncharged, substantially stereoregular backbone. A reporter in the system contains (a) a polycationic tail effective to bind electrostatically to the analyte, under conditions in which the reporter does not bind to the substantially uncharged polymers, and (b) reporter groups by which the presence of the reporter can be detected.

71. 5,216,126, Jun. 1, 1993, Receptor polypeptides and their production and uses; Edward T. Cox, et al., 530/350, 388.22, 389.1 [IMAGE AVAILABLE]
US PAT NO: 5,216,126 [IMAGE AVAILABLE] L15: 71 of

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ABSTRACT:
An isolated TGF-.beta. supergene family (TSF) receptor polypeptide is provided. This polypeptide preferably is an inhibin/activin receptor polypeptide and has at least 75% sequence identity with the mature human inhibin/activin receptor sequence. Also provided is a method for purifying TGF-.beta. supergene family members such as inhibin or activin using the polypeptide, and a method for screening for compounds with TGF-.beta. supergene family member activity by contacting the compound with the polypeptide and detecting if binding has occurred and the compound is active.

72. 5,215,882, Jun. 1, 1993, Method of immobilizing nucleic acid on a solid surface for use in nucleic acid hybridization assays; Chander Bahl, et al., 435/6, 810; 436/518, 530, 808; 935/77, 78 [IMAGE AVAILABLE]

US PAT NO: 5,215,882 [IMAGE AVAILABLE] L15: 72 of 191

ABSTRACT:
Methods of immobilizing nucleic acid on a solid surface for us in nucleic acid hybridization assays is disclosed. The methods of the invention comprise reacting a modified nucleic acid strand comprising a variable portion and an anchor portion wherein the variable portion comprises a nucleotide sequence having a selected • base • sequence and the anchor portion comprises at least one • nucleotide • • base • • modified • with a primary amine function or nucleotide • base • equivalent having a primary amine function and reacting the modified nucleic acid strand with a free aldehyde group of the solid surface in the presence of a reducing agent to form complexes of the modified nucleic acid strand and at least a portion of the free aldehyde groups on the solid surface.

73. 5,210,412, May 11, 1993, Method for analyzing an organic sample; Robert J. Levis, et al., 250/288, 282, 287 [IMAGE AVAILABLE]

US PAT NO: 5,210,412 [IMAGE AVAILABLE] L15: 73 of 191

ABSTRACT:
Described is a method and apparatus for analyzing an organic sample. In the preferred embodiment, this method and apparatus allows the determination of the • base • sequence of a nucleic acid by determining the molecular weights of the components of a biological sample. The method uses either a pre-existing chromophore or the • covalent • attachment of an ionizable chromophore to a biological sample followed by the vaporization of these molecules by exposure to an intense pulse of electromagnetic radiation in the presence of a matrix which strongly absorbs the radiation. The gaseous molecules are subsequently extracted into an evacuated ionization chamber and then exposed to electromagnetic radiation at a wavelength which specifically excites the chromophore • covalently • attached to the biological sample. The molecular weights of these ionized species are then determined by mass spectroscopic analysis. This

method of molecular weight determination allows for a DNA sequencing method. Four samples of DNA molecules are prepared such that each is • covalently • linked to an ionizable chromophore and each is fragmented by a means which results in fragments within each of the four samples that terminate at a different one of the nucleotides A, C, G or T. Each of these four fragmented samples is subsequently introduced into the said apparatus in order to determine their molecular weights hence providing the strand length of the fragments. The data generated may be analyzed by high-speed computer, the four data sets correlated, and the sequence deduced.

74. 5,208,036, May 4, 1993, N-(.omega., (.omega.-1)-dialkyloxy)- and N-(.omega., (.omega.-1)-dialkenyloxy)-alk-1-yl-N,N,N-tetrasubstituted ammonium lipids and uses therefor; Deborah A. Eppstein, et al., 424/450; 264/4.1, 4.33, 4.6; 424/422, 423, 427, 428, 449; 435/919 [IMAGE AVAILABLE]

US PAT NO: 5,208,036 [IMAGE AVAILABLE] L15: 74 of 191

ABSTRACT:

This invention relates to compounds of the formula ##STR1## or an optical isomer thereof wherein R.sup.1 and R.sup.2 are the same or different and are an alkyl or alkenyl group of 6 to 24 carbon atoms; R.sup.3, R.sup.4 and R.sup.5 are the same or different and are alkyl of 1 to 8 carbon atoms, aryl, aralkyl of 7 to 11 carbon atoms, or when two or three of R.sup.3, R.sup.4, and R.sup.5 are taken together to form quinuclidino, piperidino, pyrrolidino, or morpholino; n is 1 to 8; and X is a pharmaceutically acceptable anion.

75. 5,206,161, Apr. 27, 1993, Human plasma carboxypeptidase B; Dennis T. Drayna, et al., 435/212, 69.1 [IMAGE AVAILABLE]

US PAT NO: 5,206,161 [IMAGE AVAILABLE] L15: 75 of 191

ABSTRACT:

A novel polypeptide, designated plasma carboxypeptidase B (PCPB), has been purified from human plasma. It has been cloned from a human liver cDNA library using PCR amplification. Provided herein is nucleic acid encoding PCPB useful in diagnostics and in the recombinant preparation of PCPB. PCPB is used in the preparation and purification of antibodies thereto, in the purification of plasminogen, in the inhibition of plasminogen activation by t-PA in the presence of fibrinogen, and in diagnostic assays.

76. 5,204,456, Apr. 20, 1993, Derivatives of nucleosides and their use for the synthesis of oligonucleotides; Didier Molko, et al., 536/25.33, 26.71, 27.3, 27.5, 27.6, 27.81, 28.51 [IMAGE AVAILABLE]

US PAT NO: 5,204,456 [IMAGE AVAILABLE] L15: 76 of

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ABSTRACT:
The invention relates to derivatives of nucleosides and their use for the synthesis of oligonucleotides. These derivatives are in accordance with the formula: ##STR1## in which B represents a radical derived from guanine, cytosine or adenine, whose endocylic NH group is protected by the group ##STR2## with R.sup.1 representing a hydrogen atom or a alkyl radical and R.sup.2 a hydrogen atom, and alkyl radical, an alkoxy radical and optionally substituted aryloxy radical, R.sup.3 represents a hydrogen atom, the dimethoxytrityl radical or the radical ##STR3## R.sup.4 represents a hydrogen atom, the radical of formula: ##STR4## or a radical suitable for the synthesis of polynucelotides and R.sup.5 represents a hydrogen atom or the protected or unprotected hydroxyl OH radical.

77. 5,190,873, Mar. 2, 1993, Hybrid tryptophan aporepressor containing ligand binding sites; Waldemar Lernhardt, et al., 435/177, 69.1, 69.7; 530/350, 812; 930/250 [IMAGE AVAILABLE]

US PAT NO: 5,190,873 [IMAGE AVAILABLE] L15: 77 of 191
ABSTRACT:
Hybrid proteins containing repressor proteins and substituted receptor binding sites, amino acid and DNA sequences encoding the hybrid proteins are provided. Methods for preparing the hybrid proteins are also described.

78. 5,187,266, Feb. 16, 1993, Antitumor aldophosphamide glycoside and dideoxyuridine derivatives; David Farquhar, et al., 536/6.4, 26.8; 558/180, 199, 200; 562/10 [IMAGE AVAILABLE]

US PAT NO: 5,187,266 [IMAGE AVAILABLE] L15: 78 of 191
ABSTRACT:
A compound having the structure: ##STR1## wherein R is CH.sub.3, C.sub.2 H.sub.5, C.sub.3 H.sub.7, t-C.sub.4 H.sub.9 or C.sub.6 H.sub.5 ; R.sup.1 is NH.sub.2, NHCH.sub.3, NHC.sub.2 H.sub.5, NHC.sub.3 H.sub.7, NHC.sub.4 H.sub.9, NHCH.sub.2 CH.sub.2 Cl, NHC.sub.6 H.sub.5, N(CH.sub.3).sub.2, N(C.sub.2 H.sub.5).sub.2, N(C.sub.3 H.sub.7).sub.2, NCH.sub.3 (C.sub.2 H.sub.5), NCH.sub.3 (C.sub.3 H.sub.7), N(CH.sub.2 CH.sub.2 Cl).sub.2, NHOH, NHNHCO.sub.2 CH.sub.2 C.sub.6 H.sub.5, NHNHCO.sub.2 C(CH.sub.3).sub.3, OCH.sub.3, OC.sub.2 H.sub.5, OC.sub.3 H.sub.7, OC.sub.4 H.sub.9, OC.sub.6 H.sub.5, OC.sub.2 C.sub.6 H.sub.5, CH.sub.3, C.sub.2 H.sub.5, C.sub.3 H.sub.7, C.sub.4 H.sub.9, CH.sub.2 NO.sub.2 or CH.sub.2 NH.sub.2 ; and R.sup.2 is NHCH.sub.2 CH.sub.2 Cl or N(CH.sub.2 CH.sub.2 Cl).sub.2. These compounds may be used to eliminate occult leukemic clonogenic cells from bone marrow by contacting the bone marrow with a solution comprising levels of said compound sufficient to eliminate occult leukemic clonogenic cells. Analogously, tumor cells in a host or organ of a host may be eliminated by treatment of the host or host's organ with a compound of this description.

Compounds of this description are stable aldophosphamide analogs activatable by the action of an esterase and a subsequent E-2 elimination reaction to form acrolein and a phosphoramidic mustard of the formula: A stable aldophosphamide analog activatable by the action of an esterase and a subsequent spontaneous E-2 elimination reaction to form acrolein and a phosphoramidic mustard, said phosphoramidic mustard having the formula ##STR2## R is NH.sub.2, NHCH.sub.3, NHC.sub.2 H.sub.5, NHC.sub.3 H.sub.7, NHC.sub.4 H.sub.9, NHCH.sub.2 CH.sub.2 Cl, NHC.sub.6 H.sub.5, N(CH.sub.3).sub.2, N(C.sub.2 H.sub.5).sub.2, N(C.sub.3 H.sub.7).sub.2, NCH.sub.3 (C.sub.2 H.sub.5), NCH.sub.3 (C.sub.3 H.sub.7), N(CH.sub.2 CH.sub.2 Cl).sub.2, NHOH, NHNHCO.sub.2 CH.sub.2 C.sub.6 H.sub.5, NHNHCO.sub.2 C(CH.sub.3).sub.3, OCH.sub.3, OC.sub.2 H.sub.5, OC.sub.3 H.sub.7, OC.sub.4 H.sub.9, OC.sub.6 H.sub.5, OC.sub.2 C.sub.6 H.sub.5, CH.sub.3, C.sub.2 H.sub.5, C.sub.3 H.sub.7, C.sub.4 H.sub.9, CH.sub.2 NO.sub.2 or CH.sub.2 NH.sub.2 ; and R.sup.1 is NHCH.sub.2 CH.sub.2 Cl or N(CH.sub.2 CH.sub.2 Cl).sub.2.

79. 5,185,439, Feb. 9, 1993, Acridinium ester labelling and purification of nucleotide probes; Lyle J. Arnold, Jr., et al., 536/24.3; 435/6 [IMAGE AVAILABLE]

US PAT NO: 5,185,439 [IMAGE AVAILABLE] L15: 79 of 191

ABSTRACT:

Methods for the construction, labelling and subsequent purification of nucleic acid probes containing primary amines with acridinium esters 4-(2-succinimidyloxycarbonyl-ethyl)phenyl-10-methylacridinium-9-carboxylate fluorosulfonate). The method for attaching acridinium esters to probes uses high (0.1 to 50 mM) acridinium ester concentrations achieved using organic solvent in concentrations of 20% to 80% by volume, and may be carried out either in solution, or with one or the other of the acridinium ester or the probe suspended in solution. Purification (the separation of labelled probe from unlabelled probe and free label) involves (1) first removing most of the free acridinium ester label from probe using rapid separation techniques, then (2) removing substantially all remaining free label from the probe and separating labelled probe from unlabelled probe, involves specific applications of ion exchange, reverse phase or hydroxyapatite HPLC.

80. 5,193,885, Feb. 2, 1993, Method for chromatographic separation of synthetic phosphorothioate oligonucleotides; B. John Bergot, 536/25.41, 27.12, 55.3; 935/19 [IMAGE AVAILABLE]

US PAT NO: 5,193,885 [IMAGE AVAILABLE] L15: 80 of 191

ABSTRACT:

A method is provided for the preparation and/or analysis of synthetic phosphorothioate and -dithioate oligonucleotides. In

particular, the method permits separation of fully sulfurized phosphorothioate or -dithioate oligonucleotides from incompletely sulfurized defect species on strong-anion exchange HPLC columns using concentration gradients of novel "soft • base • " anionic eluents, such as bromide, thiocyanate, and the like.

91. 5,192,205, Jan. 26, 1993, Nucleotide sequences which are selectively expressed in pre-B cells and probes therefor; Steven R. Bauer, et al., 435/240.2, 172.3, 252.3, 252.33, 320.1; 536/23.5, 24.31 [IMAGE AVAILABLE]
US PAT NO: 5,192,205 [IMAGE AVAILABLE] L15: 91 of 191
ABSTRACT:
The present invention provides nucleotide sequences which are selectively expressed in pre-B cells, probes comprising a polynucleotide hybridizing specifically to such a nucleotide sequence and methods for the production of such probes. These probes may be used for identifying pre-B cells. The invention further provides polypeptides translated from a transcript comprising a nucleotide sequence which is selectively expressed in pre-B cells or parts thereof, antibodies against these polypeptides and methods for the preparation and use of the polypeptides and antibodies raised against them.

92. 5,192,200, Jan. 26, 1993, T-DNA promoters; Jerry L. Slightom, et al., 435/172.3, 69.1, 70.1, 240.4, 252.2, 252.3, 252.33; 536/23.2, 23.6, 24.1; 935/35, 36, 41, 67 [IMAGE AVAILABLE]

US PAT NO: 5,192,200 [IMAGE AVAILABLE] L15: 92 of 191
ABSTRACT:
The sequence of the T.sub.L -DNA of Ri plasmids found in Agrobacterium rhizogenes strains HRI and A4 is disclosed. Sixteen open reading frames bounded by eukaryotic promoters, ribosome binding sites, and polyadenylation sites were found, five of which were observed to be transcripted in a developmentally and phenotypically regulated manner. The use of promoters and polyadenylation sites from pRi T.sub.L -DNA to control expression of heterologous foreign structural genes is taught, using as examples the structural genes for Phaseolus vulgaris storage protein (phaseolin), P. vulgaris lectin, a sweet protein (thaumatin), and Bacillus thuringiensis crystal protein. Vectors useful for manipulation of sequences of the structural genes and T-DNA are also provided.
93. 5,177,198, Jan. 5, 1993, Process for preparing oligoribonucleoside and oligodeoxyribonucleoside boranophosphates; Bernard F. Spielvogel, et al., 536/25.33, 4.1, 17.1, 18.1, 25.34, 122 [IMAGE AVAILABLE]
US PAT NO: 5,177,198 [IMAGE AVAILABLE] L15: 93 of 191
ABSTRACT:
A process of making oligoribonucleoside and deoxyribonucleoside boranophosphates and salts thereof is disclosed. The process

comprises the steps of condensing a ribonucleotide or deoxyribonucleotide with a nucleoside phosphitylating agent, wherein the phosphitylating agent includes a 5' -OH group protected by an acid-labile protecting group and a moiety bonded to the phosphorus atom therein that is a stronger proton acceptor than the 5'-OH group of the ribonucleotide or deoxyribonucleotide to form a reaction intermediate, then oxidizing the reaction intermediate so formed with a compound comprising a Lewis " base " and a boron-containing substituent, wherein the Lewis " base " is a weaker electron donor than the phosphite phosphorus of the reaction intermediate, to form a ribonucleotide or deoxyribonucleotide boranophosphate. These steps are repeated on the nucleotide boranophosphate to form an oligonucleotide boranophosphate.

94. 5,177,196, Jan. 5, 1993, Oligo (.alpha.-arabinofuranosyl nucleotides) and .alpha.-arabinofuranosyl precursors thereof; Rich B. Meyer, Jr., et al., 536/22.1; 530/387.5; 536/25.3, 25.6 [IMAGE AVAILABLE]

US PAT NO: 5,177,196 [IMAGE AVAILABLE] L15: 94 of 191

ABSTRACT:

Novel oligonucleotides formed from .alpha.-D-arabinofuranosyl nucleoside monomers, including oligonucleotides in which one or more of the monomer units is functionalized, are disclosed herein, as well as functionalized monomeric .alpha.-D-arabinofuranosyl nucleosides and nucleotides. A generic formula for the oligomers is: ##STR1## in which B is a nucleotide " base " which will vary from one monomeric unit to the next in a preselected oligonucleotide sequence; R is phosphate, phsophorothioate, phosphoramidate, or alkanephosphonate; t is 1 for functionalized monomeric units and zero for the others; W is a chemical linker arm; A is a functional group; and n is the number of monomeric units in the oligomer. The oligomers are useful for diagnostic and chemotherapeutic uses. A novel reaction is also disclosed, in which an .alpha.-D-arabinofuranosyl nucleoside with exposed hydroxyls at the 2'- and 3'-positions is selectively protected at the 2'-position in a single reaction.

95. 5,177,064, Jan. 5, 1993, Targeted drug delivery via phosphonate derivatives; Nicholas S. Bodor, 514/51, 49, 50, 885; 536/6.4, 17.1, 17.5, 18.7; 552/502; 558/70 [IMAGE AVAILABLE]

US PAT NO: 5,177,064 [IMAGE AVAILABLE] L15: 95 of 191

ABSTRACT:

The invention provides compounds of the formula ##STR1## or a pharmaceutically acceptable salt thereof, wherein [D] is the residue of a drug having a reactive functional group, said functional group being attached, directly or through a bridging group, via an oxygen-phosphorus bond to the phosphorus atom of the ##STR2## moiety; R.sub.1 is C.sub.1 -C.sub.8 alkyl, C.sub.6 -C.sub.10 aryl or C.sub.7 -C.sub.12 aralkyl; R.sub.2 is hydrogen, C.sub.1 -C.sub.8 alkyl, C.sub.6 -C.sub.10 aryl, C.sub.4 -C.sub.8

heteroaryl, C.sub.3 -C.sub.7 cycloalkyl, C.sub.3 -C.sub.7 cycloheteroalkyl or C.sub.7 -C.sub.12 aralkyl; and R.sub.3 is selected from the group consisting of C.sub.1 -C.sub.8 alkyl; C.sub.2 -C.sub.8 alkenyl having one or two double bonds; (C.sub.3 -C.sub.7 cycloalkyl)--C.sub.r H.sub.2r --wherein r is zero, one, two or three, the cycloalkyl portion being unsubstituted or bearing 1 or 2 C.sub.1 -C.sub.4 alkyl substituents on the ring portion; (C.sub.6 -C.sub.10 aryloxy)C.sub.1 -C.sub.8 alkyl; 2--, 3-- or 4-- pyridyl; and phenyl-C.sub.r H.sub.2r -- wherein r is zero, one, two or three and phenyl is unsubstituted, or is substituted by 1 to 3 alkyl each having 1 to 4 carbon atoms, alkoxy having 1 to 4 carbon atoms, halo, trifluoromethyl, dialkylamino having 2 to 8 carbon atoms or alkanoylamino having 2 to 6 carbon atoms. The compounds are adapted for targeted drug delivery, especially to the brain..

96. 5,175,273, Dec. 29, 1992, Nucleic acid intercalating agents; Norbert W. Bischofberger, et al., 536/26.13, 18.7 [IMAGE AVAILABLE]

US PAT NO: 5,175,273 [IMAGE AVAILABLE] L15: 96 of 191

ABSTRACT:

Pyridinone or pyrimidinone nucleoside • bases • containing fused aromatic polycyclic rings are provided. These polycyclic nucleosides are incorporated into oligonucleotides and hybridized to complementary nucleic acid. Fluorescence spectroscopy and thermal denaturation profiles provided evidence that the polycyclic • base • is intercalated into the resulting duplex. The fused polycyclic ring systems optionally are substituted with reactive species which inactivate complementary nucleic acids. The oligonucleotides of this invention are useful as improved probes, diagnostic reagents, or for cleaving or derivatizing predetermined domains within nucleic acids.

97. 5,174,962, Dec. 29, 1992, Apparatus for determining DNA sequences by mass spectrometry; Thomas M. Brennan, 422/78; 250/281; 422/71, 80, 116; 436/59, 155, 161 [IMAGE AVAILABLE]

US PAT NO: 5,174,962 [IMAGE AVAILABLE] L15: 97 of 191

ABSTRACT:

This invention relates to the apparatus, for sequencing natural or recombinant DNA and other polynucleotides. In particular, this invention relates to a method for sequencing polynucleotides based on mass spectrometry to determine which of the four • bases • (adenine, guanine, cytosine or thymine) is a component of the terminal nucleotide. In particular, the present invention relates to identifying the individual nucleotides by the mass of stable nuclide markers contained within either the dideoxynucleotides, the DNA primer, or the deoxynucleotide added to the primer. This invention is particularly useful in identifying specific DNA sequences in very small quantities in biological products produced by fermentation or other genetic

engineering techniques. The invention is therefore useful in evaluating safety and other health concerns related to the presence of DNA in products resulting from genetic engineering techniques.

88. 5,171,844, Dec. 15, 1992, Proteins with factor VIII activity: process for their preparation using genetically-engineered cells and pharmaceutical compositions containing them; Albert J. J. van Ooyen, et al., 530/383; 435/69.6; 514/12; 530/395, 830 [IMAGE AVAILABLE]

US PAT NO: 5,171,844 [IMAGE AVAILABLE] L15: 88 of 191

ABSTRACT:

Novel polypeptides having Factor VIII activity are provided as well as compositions and methods for their preparation. The polypeptides comprise derivatives and fragments of Factor VIII and have sequences substantially similar to portions of naturally occuring Factor VIII. The polypeptides find use in treatment of Hemophilia A.

89. 5,166,387, Nov. 24, 1992, Method of synthesizing sulfurized oligonucleotide analogs with thiuram disulfides; Bernard L. Hirschbein, 558/129; 536/55.3; 548/113, 119; 568/13, 14, 15 [IMAGE AVAILABLE]

US PAT NO: 5,166,387 [IMAGE AVAILABLE] L15: 89 of 191

ABSTRACT:

A method for synthesizing sulfurized oligonucleotide analogs, such as phosphorothioate and phosphorodithioate analogs, is provided that employs a thiuram disulfide as a sulfurizing agent. The method of the invention may be used to sulfurize any phosphorous(III)-containing intermediate. Preferably, the method is practiced on a commercial DNA synthesizer using phosphoramidite and/or phosphorthioamidite intermediates.

90. 5,166,315, Nov. 24, 1992, Sequence-specific binding polymers for duplex nucleic acids; James E. Summerton, et al., 528/406, 403, 422, 423, 425 [IMAGE AVAILABLE]

US PAT NO: 5,166,315 [IMAGE AVAILABLE] L15: 90 of 191

ABSTRACT:

A polymer composition effective to bind in a sequence-specific manner to a target sequence of a duplex polynucleotide containing different Watson-Crick basepair oreientaions. The composition includes an uncharged backbone with 5- or 6-membered cyclic backbone structures and selected • bases • attached to the backbone structures effective to hydrogen bond specifically with different oriented basepairs in the target sequence.

91. 5,162,515, Nov. 10, 1992, Conjugates of biologically stable polymers and polynucleotides for treating systemic lupus erythematosus; Michael J. Conrad, et al., 536/26.1; 514/885 [IMAGE AVAILABLE]

US PAT NO: 5,162,515 [IMAGE AVAILABLE] L15: 91 of 191
ABSTRACT:
Chemically defined conjugates of biologically stable polymers, such as copolymers of D-glutamic acid and D-lysine, and polynucleotide duplexes of at least 30 • base • pairs that have significant binding activity for human lupus anti-dsDNA autoantibodies. The duplexes are preferably homogeneous in length and structure and are bound to the polymer via reaction between an amino-reactive functional group located at or proximate a terminus of each duplex. These conjugates are tolerogens for human systemic lupus erythematosus.

92. 5,162,227, Nov. 10, 1992, Recombinant DNA vectors capable of expressing apoaequorin in E. coli; Milton J. Cormier, 435/252.33, 69.1, 320.1 [IMAGE AVAILABLE]

US PAT NO: 5,162,227 [IMAGE AVAILABLE] L15: 92 of 191
ABSTRACT:
A gene which codes for the protein apoaequorin is disclosed along with recombinant DNA vectors containing this gene.

93. 5,159,095, Oct. 27, 1992, Substituted silyl alcohols; Joseph E. Celebuski, 556/436, 449 [IMAGE AVAILABLE]

US PAT NO: 5,159,095 [IMAGE AVAILABLE] L15: 93 of 191
ABSTRACT:
Novel silyl alcohols having bulky substituents bonded to the silicon, and the silyl group attached to a carbon include the preferred 2-silyl-ethan-1-ols. A method for synthesizing substituted alcohols include hydrosilation of a vinylic ester, especially vinyl acetate, followed by hydrolysis in mild • base • . The silyl alcohols are useful in preparing phosphorylating reagents for phosphorylating an oligonucleotide. The phosphorylated intermediate bearing the silyl group may be separated from failure product on the basis of bulky substituents on the silyl protecting group, which is later removed, e.g. by fluoride ion.

94. 5,153,319, Oct. 6, 1992, Process for preparing polynucleotides; Marvin H. Caruthers, et al., 536/25.3, 25.34 [IMAGE AVAILABLE]
US PAT NO: 5,153,319 [IMAGE AVAILABLE] L15: 94 of 191
ABSTRACT:
New and useful intermediate nucleotides bound to an inorganic polymer support, including the preparation thereof, and processes for the conversion to oligonucleotides which are especially useful for the synthesis of polynucleotides, particularly ribonucleic (RNA) and deoxyribonucleic (DNA) acids, are described.

95. 5,151,507, Sep. 29, 1992, Alkynylamino-nucleotides; Frank W. Hobbs, Jr., et al., 536/26.7, 27.14, 27.2, 28.52, 28.53; 544/243, 244 [IMAGE AVAILABLE]

US PAT NO: 5,151,507 [IMAGE AVAILABLE] L15: 95 of 191
ABSTRACT:

Alkynylamino-nucleotides and labeled alkynylaminonucleotides useful, for example, as chain terminating substrates for DNA sequencing are provided along with several key intermediates and processes for their preparation. For some applications, longer, hydrophilic linkers are provided.

96. 5,143,917, Sep. 1, 1992, Pharmaceutical preparations; Henrich H. Paradies, 514/256, 269, 274; 544/298, 309, 313, 315, 317 [IMAGE AVAILABLE]

US PAT NO: 5,143,917 [IMAGE AVAILABLE] L15: 96 of 191
ABSTRACT:
The synthesis and application of N(1)-n-alkyl-pyrimidinium-salts are described. These surfactants have a very small critical micelle concentration ()CMC) in the order of 10.sup.-5 -10.sup.-7 Mol/Liter. These N(1)-n-alkyl-pyrimidinium components have pharmacological activities and can act as antimetabolites.

97. 5,142,047, Aug. 25, 1992, Uncharged polynucleotide-binding polymers; James Summerton, et al., 544/118, 122, 123 [IMAGE AVAILABLE]
US PAT NO: 5,142,047 [IMAGE AVAILABLE] L15: 97 of 191
ABSTRACT:
A composition of polymer molecules effective to bind, with substantially uniform binding affinity, to a single-stranded polynucleotide containing a target sequence of • bases • . The polymer molecules are composed of a sequence of • base • -pairing moieties effective to hydrogen bond to corresponding, complementary • bases • in the target sequence, under selected binding conditions, and a predominantly uncharged, achiral backbone supporting the • base • -pairing moieties at positions and in orientations which allow hydrogen bonding between the pairing moieties of the polymer and the corresponding complementary • bases • in the target sequence. The composition has diagnostic uses, in a solid-support assay system, and therapeutic uses involving inhibition or inactivation of target polynucleotides.

98. 5,141,742, Aug. 25, 1992, Vaccines against melanoma; Joseph P. Brown, et al., 424/186.1, 277.1; 435/69.3, 70.1, 71.1, 71.2; 530/350, 395; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,141,742 [IMAGE AVAILABLE] L15: 98 of 191

ABSTRACT:
Peptides or proteins related to a melanoma associated antigen are described. These are produced in large quantities via recombinant DNA techniques and/or by chemical synthetic methods. The peptides or proteins can be used as immunogens in vaccine formulations which can induce an immune response that selectively destroys melanoma cells in a vaccinated individual. Where the peptides or proteins are expressed by a recombinant virus, inactivated or live virus vaccine formulations may be prepared.

99. 5,133,973, Jul. 28, 1992, Pharmaceutical preparations; Henrich Paradies, 424/450; 514/970; 544/309, 312, 313, 315, 317 [IMAGE AVAILABLE]

US PAT NO: 5,133,973 [IMAGE AVAILABLE] L15: 99 of 191

ABSTRACT:
The synthesis and application of N(1)-n-alkyl-pyrimidinium-salts are described. These surfactants have a very small critical micelle concentration (CMC) in the order of 10.sup.-5 -10.sup.-7 Mol/Liter. These N(1)-n-alkyl-pyrimidinium components have pharmacological activities and can act as antimetabolites.

100. 5,132,418, Jul. 21, 1992, Process for preparing polynucleotides; Marvin H. Caruthers, et al., 536/25.3, 25.34 [IMAGE AVAILABLE]

US PAT NO: 5,132,418 [IMAGE AVAILABLE] L15: 100 of 191

ABSTRACT:
This invention is a process for the production of oligonucleotides which comprises:

(a) converting an inorganic polymer into a coupling agent-polymer; (b) combining the coupling agent-polymer with a blocked nucleoside to obtain a blocked • nucleoside • - • modified • support; and (c) removing the blocking group from the blocked • nucleoside • - • modified • support to provide for the coupling of • nucleotides • to the • nucleoside • - • modified • support.

101. 5,130,238, Jul. 14, 1992, Enhanced nucleic acid amplification process; Lawrence T. Malek, et al., 435/91.21, 6, 172.3, 810; 436/94, 508; 536/23.1, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,130,238 [IMAGE AVAILABLE] L15: 101 of 191

ABSTRACT:
This invention relates to an improved process for amplifying a specific nucleic acid sequence. The process involves synthesizing single-stranded RNA, single-stranded DNA and Double-stranded DNA. The single-stranded RNA is a first template for a first primer, the single-stranded DNA is a second template for a second primer, and the double stranded DNA is a third template for synthesis of a plurality of copies of the first template. A sequence of the first primer or the second primer is complementary to a sequence of the specific nucleic acid and a sequence of the first primer

or the second primer is homologous to a sequence of the specific nucleic acid. The improvement of the amplification process involves the addition of DMSO alone or in combination with BSA, which improves the specificity and efficiency of the amplification. The amplification process may be used to increase the quantity of a specific nucleic acid sequence to allow detection, or to increase the purity of a specific nucleic acid sequence as a substitute for conventional cloning methodology.

102. 5,124,444, Jun. 23, 1992, Lactam-containing compositions and methods useful for the extraction of nucleic acids; Jeffrey Van Ness, et al., 536/25.42; 435/6; 436/178; 536/25.41; 540/451, 463, 485, 526; 546/243; 548/540, 546, 547 [IMAGE AVAILABLE]

US PAT NO: 5,124,444 [IMAGE AVAILABLE] L15: 102 of 191
ABSTRACT:
This invention relates to novel methods for the extraction of nucleic acid. In particular methods are described for isolating nucleic acid from a sample containing a complex biological mixture of nucleic acid and non-nucleic acids wherein the sample is combined with an extraction solution comprising a lactam and then the nucleic acid material is isolated from the resulting combined solution. The resulting combined solution is mixed and becomes biphasic and the nucleic acid material is isolated from the aqueous phase by precipitation with ethanol. The lactam is preferably about 5 to about 70% of the extraction solution and is most preferably 2-pyrrolidone, N-ethyl-2-pyrrolidone, N-cyclohexyl-2- pyrrolidone, N-dodecyl-2-pyrrolidone, N-methyl-2-pyrrolidone, N-hydroxyethyl-2-pyrrolidone, N-methyl-2-piperidone, 2-.epsilon.- caprolactam, N-methyl-2-caprolactam, 2-piperidone or N-(4-hydroxybenzyl)pyrrolidone. Methods for selectively isolating DNA, ribosomal RNA and plasmid DNA are also disclosed.

103. 5,122,345, Jun. 16, 1992, DNA Sequencing apparatus; Stanley Tabor, et al., 422/116; 204/182.8, 299R; 422/68.1, 69, 82.05 [IMAGE AVAILABLE]
US PAT NO: 5,122,345 [IMAGE AVAILABLE] L15: 103 of 191
ABSTRACT:
An automated DNA sequencing apparatus having a reactor for providing at least two series of DNA products formed from a single primer and a DNA strand, each DNA product of a series differing in molecular weight and having a chain terminating agent at one end; separating means for separating the DNA products to form a series bands, the intensity of substantially all nearby bands in a different series being different, band reading means for determining the position an

This invention was made with government support including a grant from the U.S. Public Health Service, contract number AI-06045. The U.S. government has certain rights in the invention.

104. 5,118,809, Jun. 2, 1992, Pharmaceutical preparations; Henrich H. Paradies, 544/309, 242, 312, 313, 315, 317 [IMAGE AVAILABLE]

US PAT NO: 5,118,809 [IMAGE AVAILABLE] L15: 104 of 191

ABSTRACT:

The synthesis and application of N(1)-n-alkyl-pyrimidinium-salts are described. These surfactants have a very small critical micelle concentration (CMC) in the order of 10.sup.-5 -10.sup.-7 Mol/Liter. These N(1)-n-alkyl-pyrimidinium components have pharmacological activities and can act as antimetabolites.

105. 5,118,802, Jun. 2, 1992, DNA-reporter conjugates linked via the 2' or 5'-primary amino group of the 5'-terminal nucleoside; Lloyd M. Smith, et al., 536/24.3, 25.32, 26.6, 27.1 [IMAGE AVAILABLE]

US PAT NO: 5,118,802 [IMAGE AVAILABLE] L15: 105 of 191

ABSTRACT:

The invention consists of compounds and methods for the synthesis of oligonucleotides which contain one or more free aliphatic amino groups attached to the sugar moieties of the nucleoside subunits. The synthetic method is versatile and general, permitting amino groups to be selectively placed at any position on oligonucleotides of any composition or length which is attainable by current DNA synthetic methods. Fluorescent dyes or other detectable moieties may be • covalently • attached to the amino groups to yield the corresponding modified oligonucleotide.

106. 5,118,800, Jun. 2, 1992, Oligonucleotides possessing a primary amino group in the terminal nucleotide; Lloyd M. Smith, et al., 536/23.1, 24.3, 25.1, 27.4 [IMAGE AVAILABLE]

US PAT NO: 5,118,800 [IMAGE AVAILABLE] L15: 106 of 191

ABSTRACT:

The invention consists of compounds and methods for the synthesis of oligonucleotides which contain one or more free aliphatic amino groups attached to the sugar moieties of the nucleoside subunits. The synthetic method is versatile and general, permitting amino groups to be selectively placed at any position on oligonucleotides of any composition or length which is attainable by current DNA synthetic methods. Fluorescent dyes or other detectable moieties may be • covalently • attached to the amino groups to yield the corresponding modified oligonucleotide.

107. 5,113,005, May 12, 1992, Process for synthesis of silyl alcohols; Joseph E. Celebuski, 556/449 [IMAGE AVAILABLE]

US PAT NO: 5,113,005 [IMAGE AVAILABLE] L15: 107 of 191

ABSTRACT:

Novel silyl alcohols having bulky substituents bonded to the silicon, and the silyl group attached to a carbon include the preferred 2-silyl-ethan-1-ols. A method for synthesizing silyl substituted alcohols include hydrosilation of a vinylic ester, especially vinyl acetate, followed by hydrolysis in mild • base • . The silyl alcohols are useful in preparing phosphorylating reagents for phosphorylating an oligonucleotide. The phosphorylated intermediate bearing the silyl group may be separated from failure product on the basis of bulky substituents on the silyl protecting group, which is later removed, e.g. by fluoride ion.

108. 5,112,844, May 12, 1992, Imidazole derivatives and use as anti-bacteria, anti-fungal and anti-viral agents; Henrich H. Paradies, 514/398, 396; 548/316.4, 335.1 [IMAGE AVAILABLE]

US PAT NO: 5,112,844 [IMAGE AVAILABLE] L15: 109 of 191
ABSTRACT:
The synthesis of quaternary five membered N-n-alkyl-heterocycles, especially of 4-hydroxy-N(1)-n-alkyl-imidazolium, 2,5-substituted N(3)-n-alkyl-thiazolium and substituted N(2) pyrazolium salts are described. The N-surfactants obtained have a very small critical micelle concentration (CMC) of 10.sup.-5 -10.sup.-7 Mol/Liter, and are capable of forming micelles of different sizes and forms depending on the nature of the anions. The N-detergents can be used as pharmaceuticals.

109. 5,110,929, May 5, 1992, Process for the preparation of N-alkylated quaternary nitrogen containing aromatic heterocycles; Henrich H. Paradies, 544/406, 408, 410 [IMAGE AVAILABLE]

US PAT NO: 5,110,929 [IMAGE AVAILABLE] L15: 109 of 191
ABSTRACT:
The synthesis of 4-, 4-(1,1)-and 3,5-substituted N-alkyl-pyridinium salts as well as of 2-carboxamide substituted N(1,4)diazinium compounds are described. The N-surfactants obtained have a small critical micelle concentration (CMC) of 10.sup.-5 -10.sup.-7 Mol/Liter. These surfactants produce micells of different size and form depending on the nature of the anions. 4-(1,1)-substituted and 3,5-substituted N-alkyl-pyridinium components are capable of forming vesicles in equeous solutions of different forms and sizes. The N-surfactants synthesized can be used as pharmaceuticals.

110. 5,109,124, Apr. 28, 1992, Nucleic acid probe linked to a label having a terminal cysteine; Kuzhalmannam L. Ramachandran, et al., 536/24.3; 435/6; 436/501; 935/16, 78, 86, 88 [IMAGE AVAILABLE]
US PAT NO: 5,109,124 [IMAGE AVAILABLE] L15: 110 of 191
ABSTRACT:

A polynucleotide probe with a label bearing a plurality of

signalling moieties. The label is attached to the probe by the reaction of an amino and sulfhydryl reactive hetero bifunctional reagent with the probe and label, the reaction resulting in the oxidation of a sulfhydryl group of the label. The label may be attached to the 5' terminus of the probe, or to modified ▼ bases ▼ of the probe. Probes constructed according to the invention are useful in detecting target sequences in genomic DNA.
111. 5,109,921, Apr. 28, 1992, Method for enhanced transmembrane transport of exogenous molecules; Philip S. Low, et al., 435/240.1, 243; 514/2, 44; 935/52 [IMAGE AVAILABLE]

US PAT NO: 5,109,921 [IMAGE AVAILABLE] L15: 111 of 191
ABSTRACT:
A method is provided for enhancing transmembrane transport of exogenous molecules. The method comprises contacting a membrane of a living cell with a complex formed between said molecules and ligands selected from biotin, biotin analogs and other biotin receptor-binding ligands, and/or folic acid, folate analogs and other folate receptor-binding ligands to initiate receptor mediated transmembrane transport of the ligand complex. The method is used for the efficient delivery of peptides, proteins, nucleic acids and other compounds capable of modifying cell function into plant, animal, yeast, and bacterial cells.

112. 5,106,730, Apr. 21, 1992, Lactam-containing compositions and methods useful for the hybridization of nucleic acids; Jeffrey Van Ness, et al., 435/6; 540/451, 463, 485, 526, 527; 546/243; 548/543, 546, 547 [IMAGE AVAILABLE]

US PAT NO: 5,106,730 [IMAGE AVAILABLE] L15: 112 of 191
ABSTRACT:
This invention relates to novel methods for the release of nucleic acids from cells in complex biological samples or specimens to prepare and make available the nucleic acid material present for a hybridization assay or for extraction. Novel methods for hybridization of nucleic acids are also presented. In particular methods are described for isolating nucleic acid from a sample containing a complex biological mixture of nucleic acid and non-nucleic acids wherein the sample is combined with a hybridization medium comprising a lactam which promotes and enables nucleic acid pairing when complementary nucleic acid is introduced. The lactam is preferably about 5 to about 70% of the hybridization medium and is most preferably 2-pyrrolidone, N-ethyl-2-pyrrolidone, N-cyclohexyl-2- pyrrolidone, N-dodecyl-2-pyrrolidone, N-methyl-2-pyrrolidone, N-hydroxyethyl-2-pyrrolidone, N-methyl-2-piperidone, 2-.epsilon.-caprolactam, N-methyl-2-caprolactam, 2-piperidone or N-(4-hydroxybenzyl)pyrrolidone.

113. 5,102,785, Apr. 7, 1992, Method of gene mapping; Kenneth J. Livak, et al., 435/6, 91.53; 436/94, 501; 935/77 [IMAGE AVAILABLE]

US PAT NO: 5,102,785 [IMAGE AVAILABLE] L15: 113 of 191
ABSTRACT:
The method described characterizes each DNA segment to be mapped by cleaving it to produce DNA fragments which are then end labeled with a reporter(s) specific to the end nuclectides of each fragment. The labeled fragments are again cleaved to produce short fragments which are separated according to size. The short fragments are analyzed as to report identify and size which is indicative of the character of each fragment. By derivatizing the cleaved ends of the primary cleaved fragments, the labeling may be delayed until the second cleavage. Prior to the labeling the derivatized fragments, all underivatized fragments are removed, the derivatized fragments being immobilized.

114. 5,093,232, Mar. 3, 1992, Nucleic acid probes; Michael S. Urdea, et al., 435/6, 7.5, 189; 536/25.32, 25.34, 26.6, 28.5, 28.52; 935/77, 78 [IMAGE AVAILABLE]

US PAT NO: 5,093,232 [IMAGE AVAILABLE] L15: 114 of 191
ABSTRACT:
• Modified • • nucleotides • are provided which have the structure ##STR1## wherein R.sup.1 is a reactive group derivatizable with a detectable label, R.sup.2 is an optional linking moiety including an amide, thioether or disulfide linkage or a combination thereof, R.sup.3 is hydrogen, methyl, bromine, fluorine or iodine, R.sup.4 is hydrogen, an acid-sensitive, • base • -stable blocking group of an acyl capping group, R.sup.5 is hydrogen or a phosphorus derivative, R.sup.6 is H, OH, or OR where R is a protecting group and x is an integer in the range of 1 and 8 inclusive. Methods of synthesizing the derivatizable nucleotide are disclosed, as are labeled polynucleotide probes prepared therefrom.
115. 5,091,552, Feb. 25, 1992, Novel antitumor aldophosphamide analogs; David Farquhar, 558/180; 536/6.4; 558/199, 200; 562/10 [IMAGE AVAILABLE]
US PAT NO: 5,091,552 [IMAGE AVAILABLE] L15: 115 of 191
ABSTRACT:
A compound having the structure: ##STR1## wherein R is CH.sub.3, C.sub.2 H.sub.5, C.sub.3 H.sub.7, t--C.sub.4 H.sub.9 or C.sub.6 H.sub.5 ; R.sup.1 is NH.sub.2, NHCH.sub.3, NHC.sub.2 H.sub.5, NHC.sub.3 H.sub.7, NHC.sub.4 H.sub.9, NHCH.sub.2 CH.sub.2 Cl, NHC.sub.6 H.sub.5, N(CH.sub.3).sub.2, N(C.sub.2 H.sub.5).sub.2, N(C.sub.3 H.sub.7).sub.2, NCH.sub.3 (C.sub.2 H.sub.5), NCH.sub.3 (C.sub.3 H.sub.7), N(CH.sub.2 CH.sub.2 Cl).sub.2, NHOH, NHNHCO.sub.2 CH.sub.2 C.sub.6 H.sub.5, NHNHCO.sub.2 C(CH.sub.3).sub.3, OCH.sub.3, OC.sub.2 H.sub.5, OC.sub.3 H.sub.7, OC.sub.4 H.sub.9, OC.sub.6 H.sub.5, OC.sub.2 C.sub.6 H.sub.5, CH.sub.3, C.sub.2 H.sub.5, C.sub.3 H.sub.7, C.sub.4 H.sub.9, CH.sub.2 NO.sub.2 or CH.sub.2 NH.sub.2 ; and R.sup.2 is NHCH.sub.2 CH.sub.2 Cl or N(CH.sub.2 CH.sub.2 Cl).sub.2. These compounds may be used to eliminate occult leukemic

clonogenic cells from bone marrow by contacting the bone marrow with a solution comprising levels of said compound sufficient to eliminate occult leukemic clonogenic cells. Analogously, tumor cells in a host or organ of a host may be eliminated by treatment of the host or host's organ with a compound of this description. Compounds of this description are stable aldophosphamide analogs activatable by the action of an esterase and a subsequent E-2 elimination reaction to form acrolein and a phosphoramidic mustard of the formula: A stable aldophosphamide analog activatable by the action of an esterase and a subsequent spontaneous E-2 elimination reaction to form acrolein and a phosphoramidic mustard, said phosphoramidic mustard having the formula ##STR2## R is NH.sub.2, NHCH.sub.3, NHC.sub.2 H.sub.5, NHC.sub.3 H.sub.7, NHC.sub.4 H.sub.9, NHCH.sub.2 CH.sub.2 Cl, NHC.sub.6 H.sub.5, N(CH.sub.3).sub.2, N(C.sub.2 H.sub.5).sub.2, N(C.sub.3 H.sub.7 (.sub.2, NCH.sub.3 (C.sub.2 H.sub.5), NCH.sub.3 C.sub.3 H.sub.7), N(CH.sub.2 CH.sub.2 Cl).sub.2, NHOH, NHNHCO.sub.2 CH.sub.2 C.sub.6 H.sub.5, NHNHCO.sub.2 C(CH.sub.3).sub.3, OCH.sub.3, OC.sub.2 H.sub.5, OC.sub.3 H.sub.7, OC.sub.4 H.sub.9, OC.sub.6 H.sub.5, OC.sub.2 C.sub.6 H.sub.5, CH.sub.3, C.sub.2 H.sub.5, C.sub.3 H.sub.7, C.sub.4 H.sub.9, CH.sub.2 NO.sub.2 or CH.sub.2 NH.sub.2 ; and R.sup.1 is NHCH.sub.2 CH.sub.2 Cl or N(CH.sub.2 CH.sub.2 Cl).sub.2.

116. 5,087,564, Feb. 11, 1992, Release of recombinant peptides from polypeptides using V8 endopeptidase; Marilyn S. Mai, et al., 435/69.7, 71.2, 172.3, 252.3, 320.1; 530/399; 536/23.2, 23.51, 23.7; 935/47, 51 [IMAGE AVAILABLE]

US PAT NO: 5,087,564 [IMAGE AVAILABLE] L15: 116 of 191
ABSTRACT:
A method for obtaining heterologous peptides from fusion proteins wherein heterologous peptides include eucaryotic hormones such as atrial peptides. A novel DNA sequence encoding atrial peptide III. Various genes, DNA vectors, endopeptidases and transformed bacteria useful in practicing the method of the present invention.

117. 5,082,934, Jan. 21, 1992, Coumarin derivatives for use as nucleotide crosslinking reagents; Don Saba, et al., 536/17.6, 17.2, 17.9, 18.1, 29.2 [IMAGE AVAILABLE]

US PAT NO: 5,082,934 [IMAGE AVAILABLE] L15: 117 of 191
ABSTRACT:
A photoactivatible • nucleoside • • analogue • is disclosed, comprising a coumarin moiety linked through its phenyl ring to the 1-position of a ribose or deoxyribose sugar moiety. The resulting • nucleoside • • analogue • is typically used as a photocrosslinking group when inserted into a polynucleotide as a replacement for one or more of the complementary nucleoside • bases • present in a probe used in a hybridization assay.

118. 5,071,974, Dec. 10, 1991, Compositions and methods for the synthesis of oligonucleotides having 5'-phosphorylated termini; E. Patrick Groody, 536/25.34, 25.3 [IMAGE AVAILABLE]

US PAT NO: 5,071,974 [IMAGE AVAILABLE] L15: 118 of 191
ABSTRACT:
Methods for the chemical 5' phosphorylation of oligonucleotides. An embodiment of the present invention includes reacting the 5' terminus of an oligonucleotide with a composition represented by the formula: ##STR1## wherein if Y and Z are taken separately, each represent an alkyl, aryl, arylalkyl, cycloalkyl or cycloalkylaryl; or if Y and Z are taken together, Y and Z form an alkyl or alkylene chain with both terminal valence bonds of said chain being attached to the nitrogen atom to which Y and Z are attached; or if Y and Z are taken together, with the nitrogen atom, Y and Z form a nitrogen heterocycle including at least one additional heteroatom selected from the group consisting of nitrogen, oxygen, and sulfur. W and X are selected from the group of functional groups subject to nucleophilic attack or .beta.-elimination and are removed.

119. 5,057,518, Oct. 15, 1991, Pharmaceutical preparations; Henrich H. Paradies, 514/274, 269, 936, 937, 970, 975; 544/242, 312, 313, 315, 317, 406; 546/265, 276, 294, 341, 347, 349; 548/178, 202, 304.4, 335.1, 347.1, 373.1 [IMAGE AVAILABLE]

US PAT NO: 5,057,518 [IMAGE AVAILABLE] L15: 119 of 191
ABSTRACT:
The synthesis and application of N(1)-n-alkyl-pyrimidinium-salts are described. These surfactants have a very small critical micelle concentration (CMC) in the order of 10.sup.-5 -10.sup.-7 Mol/Liter. These N(1)-n-alkyl-pyrimidinium components have pharmacological activities and can act as antimetabolites.

120. 5,055,459, Oct. 8, 1991, Selective elimination of malignant cells from bone marrow by bis (acyloxy) propylphosphoramidates; Borje S. Andersson, et al., 514/114, 118, 121, 129, 131 [IMAGE AVAILABLE]
US PAT NO: 5,055,459 [IMAGE AVAILABLE] L15: 120 of 191
ABSTRACT:
A method for purging tumor cells from bone marrow of a host, the method comprising

extracting bone marrow cells from the host;
treating extracted bone marrow cells with a therapeutic level of a compound having the structure: ##STR1## wherein R is CH.sub.3, C.sub.2 H.sub.5, C.sub.3 H.sub.7, t-C.sub.4 H.sub.9 or C.sub.6 H.sub.5 ; R.sup.1 is NH.sub.2, NHCH.sub.3, NHC.sub.2 H.sub.5, NHC.sub.3 H.sub.7, NHC.sub.4 H.sub.9, NHCH.sub.2 CH.sub.2 Cl, NHC.sub.6 H.sub.5, N(CH.sub.3).sub.2, N(C.sub.2 H.sub.5).sub.2, N(C.sub.3 H.sub.7).sub.2, NCH.sub.3 C.sub.2

H.sub.5), NCH.sub.3 (C.sub.3 H.sub.7), N(CH.sub.2 CH.sub.2 Cl).sub.2, NHOH, NHNHCO.sub.2 CH.sub.2 C.sub.6 H.sub.5, NHNHCO.sub.2 C(CH.sub.3).sub.3, OCH.sub.3, OC.sub.2 H.sub.5, OC.sub.3 H.sub.7, OC.sub.4 H.sub.9, OC.sub.6 H.sub.5, OCH.sub.2 C.sub.6 H.sub.5, CH.sub.3, C.sub.2 H.sub.5, C.sub.3 H.sub.7, C.sub.4 H.sub.9, CH.sub.2 NO.sub.2 or CH.sub.2 NH.sub.2; and R.sup.2 is NHCH.sub.2 CH.sub.2 Cl or N(CH.sub.2 CH.sub.2 Cl).sub.2. Intravascularly infusion of the treated bone marrow cells into the host then serves to reimplant tumor-free marrow cells.

121. 5,051,499, Sep. 24, 1991, Lipophilic 2',3'-dideoxynucleoside prodrug derivatives for the inhibition of replication of the AIDS virus and other retroviruses; Thomas I. Kalman, 536/28.2, 28.3, 28.31 [IMAGE AVAILABLE]

US PAT NO: 5,051,499 [IMAGE AVAILABLE] L15: 121 of 191
ABSTRACT:
The invention provides new alkylaminomethylene 2',3'-dideoxynucleoside compounds and salts thereof.

122. 5,051,435, Sep. 24, 1991, Pharmaceutical preparations; Henrich H. Paradies, 514/359; 548/255 [IMAGE AVAILABLE]

US PAT NO: 5,051,435 [IMAGE AVAILABLE] L15: 122 of 191
ABSTRACT:
The synthesis of quaternary five membered N-n-alkyl-hetero-cycles, especially of 4-hydroxy-N(1)-n-alkyl-imidazolium, 2,5-substituted N(3)-n-alkyl-thiazolium and substituted N(2) pyrazolium salts are described. The N-surfactants obtained have a very small critical micelle concentration (CMC) of 10.sup.-5 -10.sup.-7 Mol/Liter, and are capable of forming micelles of different sizes and forms depending on the nature of the anions. The N-detergents can be used as pharmaceuticals.

123. 5,049,386, Sep. 17, 1991, N-(.omega.,(.omega.-1)-dialkyloxy)- and N-(.omega.,(.omega.-1)-dialkenyloxy)Alk-1-YL-N,N,N-tetrasubstituted ammonium lipids and uses therefor; Deborah A. Eppstein, et al., 424/427, 449 [IMAGE AVAILABLE]

US PAT NO: 5,049,386 [IMAGE AVAILABLE] L15: 123 of 191
ABSTRACT:
This invention relates to compounds of the formula ##STR1## or an optical isomer thereof wherein R.sup.1 and R.sup.2 are the same or different and are an alkyl or alkenyl group of 6 to 24 carbon atoms; R.sup.3, R.sup.4 and R.sup.5 are the same or different and are alkyl of 1 to 8 carbon atoms, aryl, aralkyl of 7 to 11 carbon atoms, or when two or three of R.sup.3, R.sup.4, and R.sup.5 are taken together to form quinuclidino, piperidino, pyrrolidino, or morpholino; n is 1 to 8; and X is a pharmaceutically acceptable anion.

124. 5,047,519, Sep. 10, 1991, Alkynylamino-nucleotides; Frank W. Hobbs, Jr., et al., 536/27.14; 514/45; 536/27.2; 544/243, 244 [IMAGE AVAILABLE]
US PAT NO: 5,047,519 [IMAGE AVAILABLE] L15: 124 of 191
ABSTRACT:
Alkynylamino-nucleotides and labeled alkynylamino-nucleotides useful, for example, as chain terminating substrates for DNA sequencing are provided along with several key intermediates and processes for their preparation.

125. 5,045,530, Sep. 3, 1991, Pharmaceutical preparations; Henrich H. Paradies, 514/9, 10, 14, 15, 18 [IMAGE AVAILABLE]

US PAT NO: 5,045,530 [IMAGE AVAILABLE] L15: 125 of 191
ABSTRACT:

A pharmaceutical preparation is disclosed which is made up of a micelle or a vesicle each consisting of a cationic tenside with a monovalent ion and a hydrophobic cyclic or linear peptide, dispersed in a solvent whose pH value lies between pH 7-pH 8, the critical micellization concentration (cmc) lying in the range of 1.0.10.sup.-7 to 7.0.10.sup.-5 mol/liter. The preparations disclosed have in particular the advantage that by the increasing of the hydrophobicity of the alkyl or aryl chain or the radical at the N.sup.+ tenside both the membrane permeability is increased and furthermore the pharmaceutical active substance, in particular linear and cyclic tyrocidines (A-J), can be transferred actively into the cytosol. They thus act on the transciption level. In addition, linear and cyclic tyrocidines in particular have antiviral effects.

126. 5,043,272, Aug. 27, 1991, Amplification of nucleic acid sequences using oligonucleotides of random sequence as primers; James L. Hartley, 435/5, 6, 91.2, 810; 436/94, 501; 935/77, 78 [IMAGE AVAILABLE]
US PAT NO: 5,043,272 [IMAGE AVAILABLE] L15: 126 of 191
ABSTRACT:
According to this invention, a process for substantially amplifying template nucleic acid present in a sample is described, wherein said amplification may be performed without prior knowledge of specific sequences, which process comprises apposition of random oligonucleotide primers to said template nucleic acid under conditions such that extension products of said primers are synthesized which are complementary to said template nucleic acid.

127. 5,032,676, Jul. 16, 1991, Nonglycosylated analogs of human colony stimulating factors; Michael Deeley, et al., 530/351; 435/69.1, 69.5, 69.6; 530/350, 395, 820, 824; 935/49, 50 [IMAGE AVAILABLE]
US PAT NO: 5,032,676 [IMAGE AVAILABLE] L15: 127

of 191
ABSTRACT:
An analog human colony stimulating factor (hCSF) is disclosed, comprising a mutant amino acid sequence which is substantially homologous to the native sequence of an hCSF having at least one N-glycosylation site, wherein the mutant sequence comprises at least one amino acid substitution, deletion or insertion inactivating the N-glycosylation site.

128. 5,015,733, May 14, 1991, Nucleosides possessing blocked aliphatic amino groups; Lloyd M. Smith, et al., 536/27.23, 26.6, 26.8, 28.54 [IMAGE AVAILABLE]

US PAT NO: 5,015,733 [IMAGE AVAILABLE] L15: 128 of 191
ABSTRACT:
The invention consists of compounds and methods for the synthesis of oligonucleotides which contain one or more free aliphatic amino groups attached to the sugar moieties of the nucleoside subunits. The synthetic method is versatile and general, permitting amino groups to be selectively placed at any position on oligonucleotides of any composition or length which is attainable by current DNA synthetic methods. Fluorescent dyes or other detectable moieites may be • covalently • attached to the amino groups to yield the corresponding modified oligonucleotide.

129. 5,003,059, Mar. 26, 1991, Determining DNA sequences by mass spectrometry; Thomas M. Brennan, 536/25.32; 435/6, 77, 87; 536/24.3, 25.33, 25.4 [IMAGE AVAILABLE]

US PAT NO: 5,003,059 [IMAGE AVAILABLE] L15: 129 of 191
ABSTRACT:
This invention relates to the methods, apparatus, reagents and mixtures of reagents for sequencing natural or recombinant DNA and other polynucleotides. In particular, this invention relates to a method for sequencing polynucleotides based on mass spectrometry to determine which of the four • bases • (adenine, guanine, cytosine or thymine) is a component of the terminal nucleotide. In particular, the present invention relates to identifying the individual nucleotides by the mass of stable nuclide markers contained within either the dideoxynucleotides, the DNA primer, or the deoxynucleotide added to the primer. This invention is particularly useful in identifying specific DNA sequences in very small quantities in biological products produced by fermentation or other genetic engineering techniques. The invention is therefore useful in evaluating safety and other health concerns related to the presence of DNA in products resulting from genetic engineering techniques.
130. 5,002,867, Mar. 26, 1991, Nucleic acid sequence determination by multiple mixed oligonucleotide probes; Stephen J. Macevicz, 435/6, 810; 436/501, 808; 536/24.3, 24.32; 935/77, 78 [IMAGE AVAILABLE]
US PAT NO: 5,002,867 [IMAGE AVAILABLE] L15: 130

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ABSTRACT:

A method is provided for sequencing nucleic acids without the need to separate similarly sized DNAs or RNAs by gel electrophoresis. The method relies on the separate hybridization of multiple mixed oligonucleotide probes to a target sequence. The mixed oligonucleotide probes comprise sequences of fixed and non-fixed • bases • corresponding to every possible permutation of fixed and non-fixed • bases • less than or equal to the length of the probes. For each probe, the hybridizations provide the number of times the probe's particular sequence of fixed • bases • appears in the target sequence. The target sequence is then mathematically reconstructed from this data and a knowledge of the probe sequences.

131. 4,999,435, Mar. 12, 1991, N-alkyl-6,7-dihydroxy benzimidazolium salts; Henrich H. Paradies, 548/304.4; 544/113 [IMAGE AVAILABLE]
US PAT NO: 4,999,435 [IMAGE AVAILABLE] L15: 131 of 191
ABSTRACT:
The synthesis of 7-n-alkyl-imidazolium [4,5-d]-pyrimidines, 6-substituted-3n-alkyl-benzimidazolium- and 3n-alkyl-5,6-substituted- benzthiazolium salts are described. These N.sup.+ -surfactants having a substituted heterocycle as a head group have distinguished small critical micelle concentrations (CMC) in the range of 10.sup.-5 -10.sup.-7 Mol/Liter. The size and shape of these micelles in watery solutions are determined by the nature of the anion. The N-surfactants can be used as pharmaceuticals as well as reporter groups in fluorescence studies including immunological assays.

132. 4,997,928, Mar. 5, 1991, Fluorescent reagents for the preparation of 5'-tagged oligonucleotides; Frank W. Hobbs, Jr., 536/24.3; 435/6; 536/25.32, 25.34; 546/240; 549/388; 558/93, 95; 987/85 [IMAGE AVAILABLE]
US PAT NO: 4,997,928 [IMAGE AVAILABLE] L15: 132 of 191
ABSTRACT:
Fluorescent reagents possessing an activated phosphate for the convenient • covalent • coupling to the 5'-hydroxyl of oligonucleotides. A class of 5.dbd.-fluorescence-tagged oligonucleotides is also disclosed.
133. 4,987,065, Jan. 22, 1991, In vivo labelling of polynucleotide sequences; Jannis Stavrianopoulos, et al., 435/5, 6, 91.41, 172.3, 252.8, 320.1; 935/31, 58, 72, 73, 77, 78 [IMAGE AVAILABLE]

US PAT NO: 4,987,065 [IMAGE AVAILABLE] L15: 133 of 191
ABSTRACT:
In vivo labelled polynucleotides, processes for in vivo labelling of polynucleotides, and detection methods and kits characterized

by those labelled polynucleotides. The in vivo on biologically-labelled polynucleotides of this invention are useful in the detection of various analytes and in other laboratory, industrial and medical applications.
134. 4,980,460, Dec. 25, 1990, Protected nucleosides which permit more efficient oligonucleotide syntheses; Didier Molko, et al., 536/26.71, 25.31, 25.32, 26.7, 26.72, 26.8 [IMAGE AVAILABLE]

US PAT NO: 4,980,460 [IMAGE AVAILABLE] L15: 134 of 191
ABSTRACT:
The invention relates to derivatives of nucleosides and their use for the synthesis of oligonucleotides.
These derivatives are in accordance with the formula: ##STR1## in which B represents a radical derived from guanine, cytosine or adenine, whose exocylic NH group is protected by the group ##STR2## with R.sup.1 representing a hydrogen atom or an alkyl radical and R.sup.2 a hydrogen atom, and alkyl radical, an alkoxy radical and optionally substituted aryloxy radical, R.sup.3 represents a hydrogen atom, the dimethoxytrityl radical or the radical ##STR3## R.sup.4 represents a hydrogen atom, the radical of formula: ##STR4## or a radical suitable for the synthesis of polynucleotides and R.sup.5 represents a hydrogen atom or the protected or unprotected hydroxyl OH radical.

135. 4,973,679, Nov. 27, 1990, Process for oligonucleo tide synthesis using phosphormidite intermediates; Marvin H. Caruthers, et al., 536/26.71, 25.3, 26.7, 26.72 [IMAGE AVAILABLE]

US PAT NO: 4,973,679 [IMAGE AVAILABLE] L15: 135 of 191
ABSTRACT:
A new class of nucleoside phosphoramidites which are relatively stable to permit isolation thereof and storage at room temperature. The phosphoramidites are derivatives of saturated secondary amines.
136. 4,965,357, Oct. 23, 1990, 2,5,6-substituted N.sub.1 -alkylpyrimidines; Henrich H. Paradies, 544/309, 262, 296, 313, 315, 316, 317, 322, 334, 391; 546/321, 348; 548/152, 178, 202, 304.4, 335.1, 370.7, 373.1; 564/305 [IMAGE AVAILABLE]

US PAT NO: 4,965,357 [IMAGE AVAILABLE] L15: 136 of 191
ABSTRACT:
The synthesis and application of N(1)-n-alkyl-pyrimidinium-salts are described. These surfactants have a very small critical micelle concentration (CMC) in the order of 10.sup.-5 -10.sup.-7 Mol/Liter. These N(1)-n-alkyl-pyrimidinium components have pharmacological activities and can act as antimetabolites.

137. 4,965,349, Oct. 23, 1990, Method of synthesizing oligonucleotides labeled with ammonia-labile groups on solid phase supports; Sam L. Woo, et al., 536/25.3, 25.32, 25.34 [IMAGE AVAILABLE]

US PAT NO: 4,965,349 [IMAGE AVAILABLE] L15: 137 of 191
ABSTRACT:
The invention provides a novel cleavage reagent for hydrolysing • base • -labile linking groups between a solid phase support and oligonucleotides. The cleavage reagent comprises a lower alkyl alcohol, water, and a non-nucleophilic hindered alkylamine containing from 3 to 6 carbon atoms in a ratio of about 1:1:1 to about 1:3:1, respectively. An important property of the cleavage reagent is that it preserves the fluorescent characteristics of rhodamine dyes during cleavage, thereby making it possible to completely synthesize rhodamine-labeled oligonucleotides by solid phase methods. Rhodamine phosphoramidites are provided to further enhance the efficiency of synthesizing rhodamine-labeled oligonucleotides by such methods.

138. 4,959,463, Sep. 25, 1990, Intermediates; Brian C. Froehler, et al., 536/25.3, 25.32, 25.34, 25.4 [IMAGE AVAILABLE]

US PAT NO: 4,959,463 [IMAGE AVAILABLE] L15: 138 of 191
ABSTRACT:
A method is provided for the high fidelity, rapid and economical in vitro synthesis of oligonucleotides. Nucleoside H-phosphonates are condensed in seriatim using a dehydrating agent to produce a poly (nucleoside H-phosphonate). The produce is oxidized to yield the desired oligonucleotide. A novel reagent is provided for multiple nucleoside additions in single cycles.

139. 4,959,134, Sep. 25, 1990, Process and apparatus for electrophoretic determination of primary structure of nucleic acids; Valery N. Gross, et al., 204/182.8, 299R [IMAGE AVAILABLE]

US PAT NO: 4,959,134 [IMAGE AVAILABLE] L15: 139 of 191
ABSTRACT:
An apparatus and process is provided for an electrophoretic determination the primary structure of nucleic acids. The apparatus comprises a cuvette shaped as a sleeve having a gel shaped as a hollow cylinder positioned on one of the side surfaces of the sleeve and having samples of the nucleic acid in recesses on its end face located in a circle. The sleeve is provided with a rotation drive and its side wall and the bottom together with the side wall and the bottom of the second sleeve mounted coaxially with the first sleeve form chambers for placing electrode solutions therein. Between the electrode solutions in the region between the side walls of the sleeves there is located a non-polar liquid, its density is higher than that of the electrode solution located above it and lower than the density of the electrode solution located thereunder. In the chambers annular electrodes are provided and a heat-exchanger in the non-polar liquid which maintains, through the non-polar liquid, the temperature of the gel shaped as a hollow cylinder at a

predetermined level.

140. 4,958,013, Sep. 18, 1990, Cholesteryl modified oligonucleotides; Robert L. Letsinger, 536/24.5, 5, 25.1, 26.22 [IMAGE AVAILABLE]
US PAT NO: 4,958,013 [IMAGE AVAILABLE] L15: 140 of 191
ABSTRACT:

Oligonucleotides modified at their backbones by the attachment of cholesteryl are described. The modified oligonucleotides anchor in the cell membrane to serve as a probe and to provide therapeutic activity.

141. 4,948,882, Aug. 14, 1990, Single-stranded labelled oligonucleotides, reactive monomers and methods of synthesis; Jerry L. Ruth, 536/25.32; 435/6; 536/24.3, 25.33, 25.34, 26.6, 26.7, 26.8; 935/77, 78 [IMAGE AVAILABLE]

US PAT NO: 4,948,882 [IMAGE AVAILABLE] L15: 141 of 191
ABSTRACT:
Substantially pure single-stranded oligonucleotides having a preselected sequence of not more than about 200 nucleotides, at least one of which is at a preselected position in the sequence and includes a ▼ base ▼ with a ▼ covalently ▼ attached linker arm containing or capable of binding at least one reporter group or solid support. A process for the chemical synthesis of the substantially pure single-stranded oligonucleotide and ▼ modified ▼ ▼ nucleosides ▼ useful in such synthesis are provided.

142. 4,946,787, Aug. 7, 1990, N-(.omega.,(.omega.-1)-dialkyloxy)- and N-(.omega.,(.omega.-1)-dialkenyloxy)-alk-1-yl-N,N,N-tetrasubstituted ammonium lipids and uses therefor; Deborah A. Eppstein, et al., 435/240.2; 264/4.1, 4.6; 424/450 [IMAGE AVAILABLE]

US PAT NO: 4,946,787 [IMAGE AVAILABLE] L15: 142 of 191
ABSTRACT:
This invention relates to compounds of the formula ##STR1## or an optical isomer thereof wherein R.sup.1 and R.sup.2 are the same or different and are an alkyl or alkenyl group of 6 to 24 carbon atoms; R.sup.3, R.sup.4 and R.sup.5 are the same or different and are alkyl of 1 to 8 carbon atoms, aryl, aralkyl of 7 to 11 carbon atoms, or when two or three of R.sup.3, R.sup.4, and R.sup.5 are taken together to form quinuclidino, piperidino, pyrrolidino, or morpholino; n is 1 to 8; and X is a pharmaceutically acceptable anion.

143. 4,923,901, May 8, 1990, Membranes with bound oligonucleotides and peptides; Hubert Koester, et al., 521/53; 428/305.5; 536/25.3, 25.34, 27.1; 562/553, 561 [IMAGE AVAILABLE]

US PAT NO: 4,923,901 [IMAGE AVAILABLE] L15: 143

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ABSTRACT:
A method is provided for synthesizing oligonucleotides and peptides directly onto a membrane. The method provides a means for generating membrane affinity supports. A modified membrane for the method of direct synthesis is also provided.

144. 4,910,300, Mar. 20, 1990, Method for making nucleic acid probes; Michael S. Urdea, et al., 536/26.8; 435/6; 536/28.5, 28.52 [IMAGE AVAILABLE]

US PAT NO: 4,910,300 [IMAGE AVAILABLE] L15: 144 of 191
ABSTRACT:
▼ Modified ▼ ▼ nucleotides ▼ are provided which have the structure ##STR1## wherein R.sup.1 is a reactive group derivatizabale with a detectable label, R.sup.2 is an optional linking moiety including an amide, thioether or disulfide linkage or a combination thereof. R.sup.3 is hydrogen, methyl, bromine, fluorine or iodine, R.sup.4 is hydrogen, an acid-sensitive, ▼ base ▼ -stable blocking group or an acyl capping group, R.sup.5 is hydrogen or a phosphorus derivative, R.sup.6 is H, OH, or OR where R is a protecting group and n is an integer in the range of 1 and 9 inclusive. Methods of synthesizing the derivatizable nucleotide are disclosed, as are labeled polynucleotide probes prepared therefrom.
145. 4,897,355, Jan. 30, 1990, N[.omega.,(.omega.-1)-dialkyloxy]- and N-[.omega.,(.omega.-1)-dialkenyloxy]-alk-1-yl-N,N,N-tetrasubstituted ammonium lipids and uses therefor; Deborah A. Eppstein, et al., 435/240.2 [IMAGE AVAILABLE]

US PAT NO: 4,897,355 [IMAGE AVAILABLE] L15: 145 of 191
ABSTRACT:
This invention relates to compounds of the formula ##STR1## or an optical isomer thereof wherein R.sup.1 and R.sup.2 are the same or different and are an alkyl or alkenyl group of 6 to 24 carbon atoms; R.sup.3, R.sup.4 and R.sup.5 are the same or different and are alkyl of 1 to 8 carbon atoms, aryl, aralkyl of 7 to 11 carbon atoms, or when two or three of R.sup.3, R.sup.4, and R.sup.5 are taken together to form quinuclidino, piperidino, pyrrolidino, or morpholino; n is 1 to 8; and X is a pharmaceutically acceptable anion.

146. 4,894,454, Jan. 16, 1990, Pharmaceutical preparations; Henrich H. Paradies, 544/406, 232, 408, 410 [IMAGE AVAILABLE]

US PAT NO: 4,894,454 [IMAGE AVAILABLE] L15: 146 of 191
ABSTRACT:
The synthesis of 4-, 4-1,1- and 3,5- substituted N-alkyl-pyridinium salts as well as of 2-carbonamide substituted N 1,4 diazinium compounds are described. The N-surfactants

obtained have a small critical micelle concentration (CMC) of 10.sup.-5 -10.sup.-7 Mol/Liter. These surfactants produce micells of different size and form depending on the nature of the anions. 4-(1,1)-substituted and 3,5-substituted N-alkyl-pyridinium components are capable of forming vesicles in equeous solutions of different forms and sizes. The N-surfactants synthesized can be used as pharmaceuticals.

147. 4,883,750, Nov. 28, 1989, Detection of specific sequences in nucleic acids; Norman M. Whiteley, et al., 435/6, 803; 436/811; 536/24.3; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,883,750 [IMAGE AVAILABLE] L15: 147 of 191
ABSTRACT:
The invention provides a method for diagnosis of genetic abnormalities or other genetic conditions which can be readily automated. The method is used to determine the presence or absence of a target sequence in a sample of denatured nucleic acid and entails hybridizing the sample with a probe complementary to a diagnostic portion of the target sequence (the diagnostic probe), and with a probe complementary to a nucleotide sequence contiguous with the diagnostic portion (the contiguous probe), under conditions wherein the diagnostic probe remains bound substantially only to the sample nucleic acid containing the target sequence. The diagnostic probe and contiguous probe are then • covalently • attached to yield a target probe which is complementary to the target sequence, and the probes which are not attached are removed. In the preferred mode, one of the probes is labeled so that the presence or absence of the target sequence can then be tested by melting the sample nucleic acid-target probe duplex, eluting the dissociated target probe, and testing for the label. In another embodiment, the testing is accomplished without first removing probes not • covalently • attached, by attaching a hook to the probe that is not labeled, so that the labeled target probe may be recovered by catching the hook. In both instances, the presence of both the diagnostic probe and the contiguous probe is required for the label to appear in the assay. The above method is then applied to the detection of genetic diseases.

148. 4,882,435, Nov. 21, 1989, Pharmaceutical preparations; Heinrich H. Paradies, 548/127 [IMAGE AVAILABLE]

US PAT NO: 4,882,435 [IMAGE AVAILABLE] L15: 148 of 191
ABSTRACT:
The synthesis of quaternary five membered N-n-alkyl-heterocycles, especially of 4-hydroxy-N(1)-n-alkyl-imidazolium, 2,5-substituted N(3)-n-alkyl-thiazolium and substituted N(2) pyrazolium salts are described. The N-surfactants obtained have a very small critical micelle concentration (CMC) of 10.sup.-5 -10.sup.-7 Mol/Liter, and are capable of forming micelles of different sizes and forms depending on the nature of the anions. The N-detergents can be

used as pharmaceuticals.
149. 4,882,269, Nov. 21, 1989, Amplified hybridization assay; Robert J. Schneider, et al., 435/6, 18, 21, 803, 810; 436/800, 805, 808; 536/24.3, 24.31, 24.32; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,882,269 [IMAGE AVAILABLE] L15: 149 of 191
ABSTRACT:

An amplified hybridization assay is described in which a family of signal-generating secondary probes bind to a primary probe that hybridizes to the target sequence of interest. Thus, an enormously amplified signal is generated by the hybridization event. The assay can be used for a variety of laboratory and clinical purposes and is automatable.

150. 4,877,883, Oct. 31, 1989, Substituted pyrazoles; Henrich H. Paradies, 548/370.7, 127, 182, 183, 202, 225, 226, 229, 235, 255, 373.1 [IMAGE AVAILABLE]

US PAT NO: 4,877,893 [IMAGE AVAILABLE] L15: 150 of 191
ABSTRACT:
The synthesis of quaternary five membered N-n-alkyl-heterocycles, especially of 4-hydroxy-N(1)-n-alkyl-imidazolium, 2,5-substituted N(3)-n-alkyl-thiazolium and substituted N(2) pyrazolium salts are described. The N-surfactants obtained have a very small critical micelle concentration (CMC) of 10.sup.-5 -10.sup.-7 Mol/Liter, and are capable of forming micelles of different sizes and forms depending on the nature of the anions. The N-detergents can be used as pharmaceuticals.
151. 4,874,850, Oct. 17, 1989, Pharmaceutical preparations; Henrich H. Paradies, 536/3; 546/290, 321, 347; 548/179, 304.4, 336.1, 370.7, 373.1 [IMAGE AVAILABLE]

US PAT NO: 4,874,850 [IMAGE AVAILABLE] L15: 151 of 191
ABSTRACT:
A pharmaceutical preparation is disclosed which is made up of a micelle or a vesicle each consisting of a cationic tenside with a monovalent ion and a hydrophobic cyclic or linear peptide, dispersed in a solvent whose pH value lies between pH 7-pH 9, the critical micellization concentration (cmc) lying in the range of 1.0 . 10.sup.-7 to 7.0 . 10.sup.-5 mol/liter. The preparation disclosed have in particular the advantage that by the increasing of the hydrophobicity of the alkyl or aryl chain or the radical at the N.sup.+ tenside both the membrane permeability is increased and furthermore the pharmaceutical active substance, in particular linear and cyclic tyrocidines (A-E), can be transferred actively into the cytosol. They thus act on the transcription level. In addition, linear and cyclic tyrocidines in particular have antiviral effects.

152. 4,870,174, Sep. 26, 1989, Imidazopyrionidines and their use

in pharmaceutical preparations; Henrich H. Paradies, 544/273, 112, 242, 265, 267, 309, 311, 313, 334, 407; 546/255, 267, 290, 347; 548/152, 178, 202, 304.4, 335.1, 370.7, 373.1 [IMAGE AVAILABLE]

US PAT NO: 4,870,174 [IMAGE AVAILABLE] L15: 152 of 191
ABSTRACT:
The synthesis of 7-n-alkyl-imidazolium[4,5-d]-pyrimidines, 6-substituted-3n-alkyl-benzimidazolium- and 3n-alkyl-5,6-substituted- benzthiazolium salts are described. There N.sup.+ -surfactants having a substituted heterocycle as a head group have distinguished small critical micelle concentrations (CMC) in the range of 10.sup.-5 -10.sup.-7 Mol/Liter. The size and shape of these micelles in watery solutions are determined by the nature of the anion. The N-surfactants can be used as pharmaceuticals as well as reporter groups in fluorescence studies including immunological assays.

153. 4,868,103, Sep. 19, 1989, Analyte detection by means of energy transfer; Jannis Stavrianopoulos, et al., 435/5, 6, 803; 436/501, 518, 528, 536, 537, 800, 805, 821; 536/24.3; 935/78 [IMAGE AVAILABLE]
US PAT NO: 4,868,103 [IMAGE AVAILABLE] L15: 153 of 191
ABSTRACT:
A method is disclosed to detect the presence of an analyte. The method involves forming a complex comprising the analyte and a binding entity. The binding entity comprises a first partner of an energy transfer system. The complex is then contacted with a reporting entity to form a unit. The reporting entity comprises a second partner of the energy transfer system. The first partner and the second partner are within Furster's radius of each other in the formed unit. The unit is irradiated with energy which can only be absorbed by one of said partners, namely, the energy donor, which then emits fluorescent energy. Some of this energy is absorbed by the other of said partners, namely, the energy acceptor, which also emits fluorescent energy. However, the fluorescent energy of the energy acceptor is of longer wavelength and in addition may be of substantially greater duration than the fluorescent energy of the energy donor. The detection of fluorescence at the longer wavelength or after a given time interval verifies the presence of the analyte.
154. 4,849,513, Jul. 18, 1989, Deoxyribonucleoside phosphoramidites in which an aliphatic amino group is attached to the sugar ring and their use for the preparation of oligonucleotides containing aliphatic amino groups; Lloyd M. Smith, et al., 536/26.6, 25.32, 25.34, 26.8, 28.53, 28.54 [IMAGE AVAILABLE]

US PAT NO: 4,849,513 [IMAGE AVAILABLE] L15: 154 of 191
ABSTRACT:

The invention consists of compounds and methods for the synthesis of oligonucleotides which contain one or more free aliphatic amino groups attached to the sugar moieties of the nucleoside subunits. The synthetic method is versatile and general, permitting amino groups to be selectively placed at any position on oligonucleotides of any composition or length which is attainable by current DNA synthetic methods. Fluorescent dyes or other detectable moieties may be • covalently • attached to the amino groups to yield the corresponding modified oligonuclectide.

155. 4,839,290, Jun. 13, 1989, Process for producing cytotonic T-cells and compositions produced by said process; Takeji Kaieda, et al., 435/240.23, 1, 2, 240.2 [IMAGE AVAILABLE]

US PAT NO: 4,839,291 [IMAGE AVAILABLE] L15: 155 of 191
ABSTRACT:

A method of inducing antitumor immunocytes which is simple in operation and suitable for inducing antitumor immunocytes having not only excellent cytotonic activity against tumor cells but also high safety, which method comprises contacting leucocytes with an insoluble, antitumor immunocyte-inducing material capable of linking with T cells, said antitumor immunocyte-inducing material comprising an insoluble carrier and a ligand linked therewith. The induced antitumor immunocytes can be simply separated in substantially ligand-free form from the insoluble, antitumor immunocyte-inducing material. The obtained antitumor immunocytes have not only excellent cytotonic activity against tumor cells but also high safety.

156. 4,833,084, May 23, 1989, Monoclonal antibody specific for DNA.RNA hybrids; Robert J. Carrico, 530/388.21; 435/6, 240.27; 436/548; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,833,084 [IMAGE AVAILABLE] L15: 156 of 191
ABSTRACT:
A monoclonal antibody specific for DNA.multidot.RNA duplexes, particularly DNA.multidot.RNA heteropolymer duplexes, characterized by having cross-reactivity for binding to single- or double-stranded DNA or RNA as measured by competitive immunoassay of less than about 1:1000, and preferably less than 1:10,000, and an affinity for DNA.multidot.RNA heteropolymer duplexes greater than 10.sup.9 L/mole. The monoclonal antibody is prepared by conventional somatic cell hybridization techniques wherein the host animal is preferably immunized with an immunogen comprising a random DNA.multidot.RNA heteropolymer. The antibody, particularly in a labeled form, is useful in the specific detection of DNA.multidot.RNA duplexes in a test medium such as a nucleic acid hybridization assay mixture.

157. 4,828,979, May 9, 1989, • Nucleotide • • analogs • for nucleic acid labeling and detection; Leonard Klevan, et al.,

435/6; 536/24.3, 25.32, 26.6, 26.7, 26.8 [IMAGE AVAILABLE]

US PAT NO: 4,828,979 [IMAGE AVAILABLE] L15: 157 of 191
ABSTRACT:
▼ Nucleotide ▼ ▼ analogs ▼ , ▼ modified ▼ by the attachment at hydrogen bonding positions of linker groups, that is, the 6-position of adenine, 4-position of cytosine, and 2-position of guanine, are prepared. Such analogs, alone or with reporter groups attached, may be incorporated into DNA probes which effectively hybridize to target DNA.

158. 4,822,731, Apr. 18, 1989, Process for labeling single-stranded nucleic acids and hybridizaiton probes; Robert M. Watson, et al., 435/6; 436/501, 827; 536/24.3, 25.32, 25.4, 25.5, 25.6; 930/10; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,822,731 [IMAGE AVAILABLE] L15: 158 of 191
ABSTRACT:
Nucleic acids may be labeled by complexing the alkylating moiety of a labeling reagent into a single-stranded nucleic acid to form a complex and activating the complex to cause ▼ covalent ▼ bonding between the reagent and the nucleic acid. Preferably, the labeled nucleic acid is a single-stranded hybridization probe for detecting nucleic acid sequences capable of hybridizing with a hybridizing region of the nucleic acid. Also preferably the label moiety is non-radioactive. The labeling reagent is of the formula:

[A--[B--L
where A is an alkylating moiety, B is a divalent organic moiety of the formula: ##STR1## where Y is O, NH or N--CHO, x is a number from 1 to 4, y is a number from 2 to 4, and L is a monovalent label moiety, wherein B is exclusive of any portion of the alkylating and label moieties. Preferably A is a 4-methylene-substituted psoralen moiety, and most preferably A is a 4'-methylene-substituted-4,5',8-trimethylpsoralen moiety and L is biotin.

159. 4,818,681, Apr. 4, 1989, Fast and specific immobilization of nucleic acids to solid supports; Nanibhushan Dattagupta, 435/6, 91.5; 436/94; 536/24.31, 25.3, 25.4; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,818,681 [IMAGE AVAILABLE] L15: 159 of 191
ABSTRACT:
A process for synthesizing an oligonucleotide comprising linking a nucleoside phosphate to a solid support, through the heterocyclic moiety of the nucleoside, coupling a mono- or oligonucleotide to the nucleoside phosphate through its phosphate moiety, in at least one step enzymatically lengthening the mono- or oligonucleotide, cleaving the resultant oligonucleotide from

the solid support-nucleoside phosphate at the phosphate moiety of the nucleoside, and separating the oligonucleotide. After cleaving and separating the solid support-nucleoside phosphate is recycled for further coupling. Advantageously the solid support-nucleoside phosphate is phosphorylated between separation and recycling.

160. 4,812,394, Mar. 14, 1989, Flow cytomeric measurement of DNA and incorporated ▼ nucleoside ▼ ▼ analogs ▼ ; Frank A. Dolbeare, et al., 435/6, 7.21, 7.23, 29, 91.1, 810; 436/517, 518, 810; 536/23.1; 935/77, 109 [IMAGE AVAILABLE]

US PAT NO: 4,812,394 [IMAGE AVAILABLE] L15: 160 of 191
ABSTRACT:

A method is provided for simultaneously measuring total cellular DNA and incorporated ▼ nucleoside ▼ ▼ analog ▼ . The method entails altering the cellular DNA of cells grown in the presence of a ▼ nucleoside ▼ ▼ analog ▼ so that single stranded and double stranded portions are present. Separate stains are used against the two portions. An immunochemical stain is used against the single stranded portion to provide a measure of incorporated ▼ nucleoside ▼ ▼ analog ▼ , and a double strand DNA-specific stain is used against the double stranded portion to simultaneously provide a measure of total cellular DNA. The method permits rapid flow cytometric analysis of cell populations, rapid identification of cycling and noncycling subpopulations, and determination of the efficacy of S phase cytotoxic anticancer agents.

161. 4,803,297, Feb. 7, 1989, Carbamic acid ester useful for preparing a nucleic acid probe; Corey H. Levenson, et al., 560/159 [IMAGE AVAILABLE]
US PAT NO: 4,803,297 [IMAGE AVAILABLE] L15: 161 of 191
ABSTRACT:
Nucleic acids may be labeled by intercalating the alkylating intercalation moiety of a labeling reagent into a partially double-stranded nucleic acid to form a complex and activating the complex to cause ▼ covalent ▼ bonding between the reagent and the nucleic acid. Preferably, the labeled nucleic acid is hybridization probe for detecting nucleic acid sequences capable of hybridizing with a hybridizing region of the nucleic acid. Also preferably the label moiety is non-radioactive. The labeling reagent is of the formula:

[A--[B--L

where A is an alkylating intercalation moiety, B is a divalent organic moiety of the formula: ##STR1## where Y is O, NH or N--CHO, n is a number from 1 to 4, y is a number from 2 to 4, and L is a monovalent label moiety, wherein B is exclusive of any portion of the intercalation and label moieties. Preferably A is a 4-methylene-substituted psoralen moiety, and most preferably A is a

4'-methylene-substituted-4,5',8-trimethylpsoralen moiety and L is biotin.

162. 4,772,548, Sep. 20, 1988, Radioisotopicassay using isotope transfer to chelator-target recognition molecule conjugate; Jannis G. Stavrianpoulos, 435/5; 424/94.1; 435/7.2, 7.21, 7.25, 7.31, 7.32, 7.4, 7.5, 7.8, 810; 436/518, 531, 542, 545, 804, 808; 530/402, 403, 405, 406; 536/5, 22.1 [IMAGE AVAILABLE]

US PAT NO: 4,772,548 [IMAGE AVAILABLE] L15: 162 of 191
ABSTRACT:
A method of forming a therapeutic or diagnostic agent labeled with a radioactive metal ion, which comprises: contacting an unlabeled therapeutic or diagnostic agent, consisting of a substantially non-metal chelating portion and a chelating portion capable of chelating with the radioactive metal ion, with an ion transfer material having the radioactive metal ion bound thereto and having a binding affinity for the radioactive metal less than the binding affinity of the chelating portion for the radioactive metal ion, wherein prior to contacting the chelating portion is unchelated or is chelated with a second metal having a binding affinity with the chelating portion less than the binding affinity of the radioactive metal ion, whereby a radiolabeled therapeutic or diagnostic agent is formed by the contacting, and separating the radiolabeled therapeutic or diagnostic agent from the ion transfer material, is disclosed along with various components and kits useful in practicing this method and several variations thereof.

163. 4,767,609, Aug. 30, 1988, Therapeutic and diagnostic processes using isotope transfer to chelator-target recognition molecule conjugate; Jannis G. Stavrianpoulos, 424/1.45; 206/569, 570; 422/61; 424/1.53, 1.57, 1.69, 1.73, 179.1, 179.1; 514/44; 530/350, 402, 403, 405, 406; 536/24.3, 24.31 [IMAGE AVAILABLE]

US PAT NO: 4,767,609 [IMAGE AVAILABLE] L15: 163 of 191
ABSTRACT:
A method of forming a therapeutic or diagnostic agent labeled with a radioactive metal ion, which comprises: contacting an unlabeled therapeutic or diagnostic agent, consisting of a substantially non-metal chelating portion and a chelating portion capable of chelating with the radioactive metal ion, with an ion transfer material having the radioactive metal ion bound thereto and having a binding affinity for the radioactive metal less than the binding affinity of the chelating portion for the radioactive metal ion, wherein prior to contacting the chelating portion is unchelated or is chelated with a second metal having a binding affinity with the chelating portion less than the binding affinity of the radioactive metal ion, whereby a radiolabeled therapeutic or diagnostic agent is formed by the contacting, and separating the radiolabeled therapeutic or diagnostic agent from the ion transfer material, is disclosed along with various

components and kits useful in practicing this method and several variations thereof.

164. 4,766,064, Aug. 23, 1988, Displacement polynucleotide assay employing polyether and diagnostic kit; Jon I. Williams, et al., 435/6, 803, 810; 436/501; 536/24.3; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,766,064 [IMAGE AVAILABLE] L15: 164 of 191
ABSTRACT:
A diagnostic reagent is disclosed containing a complex of a probe polynucleotide (P) bound via purine/pyrimidine hydrogen bonding to a labeled polynucleotide (L). The probe (P) contains a target binding region (TBR) capable of binding to a target nucleotide sequence (G) of a biological sample. A method is disclosed in which contact with a sample containing the target nucleotide sequence (G) causes binding, initially between G and a single-stranded portion (IBR) of the target binding region (TBR). Thereafter the labeled polynucleotide (L) is displaced from the complex by branch migration of (G) into the (P)/(L) binding region. A volume excluding polymeric agent such as poly(ethylene oxide) (PEO or PEG) or other polyethers enhances the rate of appearance of displaced labeled polynucleotide. Determination of displaced labeled polynucleotide (L) gives a value which is a function of the presence and concentration of target nucleotide sequence (G) in the sample.

165. 4,766,062, Aug. 23, 1988, Displacement polynucleotide assay method and polynucleotide complex reagent therefor; Steven E. Diamond, et al., 435/6, 803, 810; 436/501; 536/24.3; 935/78 [IMAGE AVAILABLE]
US PAT NO: 4,766,062 [IMAGE AVAILABLE] L15: 165 of 191
ABSTRACT:
A diagnostic reagent is disclosed containing a complex of a probe polynucleotide (P) bound via purine/pyrimidine hydrogen bonding to a labeled polynucleotide (L). The probe (P) contains a target binding region (TBR) capable of binding to a target nucleotide sequence (G) of a biological sample. A method is disclosed in which contact with a sample containing the target nucleotide sequence (G) causes binding, initially between G and a single-stranded portion (IBR) of the target binding region (TBR). Thereafter the labeled polynucleotide (L) is displaced from the complex by branch migration of (G) into the (P)/(L) binding region. Determination of displaced labeled polynucleotide (L) gives a value which is a function of the presence and concentration of target nucleotide sequence (G) in the sample.

166. 4,754,065, Jun. 28, 1988, Precursor to nucleic acid probe; Corey H. Levenson, et al., 562/564 [IMAGE AVAILABLE]

US PAT NO: 4,754,065 [IMAGE AVAILABLE] L15: 166 of 191
ABSTRACT:

Nucleic acids may be labeled by intercalating the alkylating intercalation moiety of a labeling reagent into a partially double-stranded nucleic acid to form a complex and activating the complex to cause • covalent • bonding between the reagent and the nucleic acid. Preferably, the labeled nucleic acid is a hybridization probe for detecting nucleic acid sequences capable of hybridizing with a hybridizing region of the nucleic acid. Also preferably the label moiety is non-radioactive. The labeling reagent is of the formula:
[A] [B] L
where A is an alkylating intercalation moiety, B is a divalent organic moiety of the formula: ##STRI## where Y is O, NH or N--CHO, x is a number from 1 to 4, y is a number from 2 to 4, and L is a monovalent label moiety, wherein B is exclusive of any portion of the intercalation and label moieties.
Preferably A is a 4-methylene-substituted psoralen moiety, and most preferably A is a
4'-methylene-substituted-4,5',8-trimethylpsoralen moiety and L is biotin.

167. 4,753,884, Jun. 28, 1988, Pseudorabies virus mutants, vaccines containing same, methods for the production of same and methods for the use of same; Malon Kit, et al., 424/205.1, 229.1, 815, 822; 435/172.1, 172.3, 236, 320.1; 536/23.1; 935/65 [IMAGE AVAILABLE]

US PAT NO: 4,753,884 [IMAGE AVAILABLE] L15: 167 of 191
ABSTRACT:
The present invention relates to pseudorabies virus mutants containing deletion and/or insertion mutations in a major viral glycoprotein gene, such that no antigenic polypeptides encoded by the viral gene are produced. As a result, animals vaccinated with such do not develop antibodies to the viral glycoprotein and can be distinguished from animals infected with pseudorabies virus field strains and known pseudorabies virus vaccine strains. The present invention also relates to vaccines for pseudorabies disease containing the same, methods for production of the same and methods for use of the same.

168. 4,751,313, Jun. 14, 1988, Precursor to nucleic acid probe; Corey H. Levenson, et al., 548/304.1 [IMAGE AVAILABLE]

US PAT NO: 4,751,313 [IMAGE AVAILABLE] L15: 168 of 191
ABSTRACT:
Nucleic acids may be labeled by intercalating the alkylating intercalation moiety of a labeling reagent into a partially double-stranded nucleic acid to form a complex and activating the complex to cause • covalent • bonding between the reagent and the nucleic acid. Preferably, the labeled nucleic acid is a hybridization probe for detecting nucleic acid sequences capable of hybridizing with a hybridizing region of the nucleic acid. Also preferably the label moiety is non-radioactive. The labeling

reagent is of the formula:
[A][B]L
where A is an alkylating intercalation moiety, B is a divalent organic moiety of the formula: ##STR1## where Y is O, NH or N--CHO, n is a number from 1 to 4, y is a number from 2 to 4, and L is a monovalent label moiety, wherein B is exclusive of any portion of the intercalation and label moieties.
Preferably A is a 4-methylene-substituted psoralen moiety, and most preferably A is a 4'-methylene-substituted-4,5',8-trimethylpsoralen moeity and L is biotin.

169. 4,749,647, Jun. 7, 1988, Polymerization-induced separation assay using recognition pairs; Elaine K. Thomas, et al., 435/5, 6, 7.21, 7.32, 7.4, 7.8, 7.92, 7.94; 436/501, 504, 538, 539, 548, 827; 525/904; 526/238.1; 527/202; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,749,647 [IMAGE AVAILABLE] L15: 169 of 191
ABSTRACT:
Methods and compounds are disclosed for determining the presence, amount of, or association between substances of interest in samples suspected of containing same. The methods are based on the polymerization-induced separation of specifically-bound, reporter-labeled recognition reactants from free, reporter-labeled recognition reactants. The methods described are applicable to any substance for which suitable recognition reactants exist or can be made and are not limited by considerations such as chemical composition or molecular size.

170. 4,743,535, May 10, 1988, Hybridization assay employing labeled probe and anti-hybrid; Robert J. Carrico, 435/6, 810; 436/501, 536, 537, 805, 809; 536/24.3; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,743,535 [IMAGE AVAILABLE] L15: 170 of 191
ABSTRACT:

A nucleic acid hybridization assay involving a labeled probe and formation of a hybrid having epitopes for an antibody reagent. The label provides a detectable response which is measurably different when the labeled probe is comprised in a hybrid that is bound by the antibody reagent compared to when not comprised in such a hybrid. Particularly useful antibody reagents are antibodies such as anti-DNA.RNA, anti-RNA.RNA and antibodies to intercalated duplexes which do not bind substantially to single stranded nucleic acids. Modulation of the label response can be accomplished in a variety of ways such as by steric inactivation or hindrance or by labeling the antibody reagent with a second label which interacts with the first label. The assay is particularly advantageous because no separation of hybridized and unhybridized probe is required.

171. 4,732,859, Mar. 22, 1988, Method for conferring

bacteriophage resistance to bacteria; Charles L. Hershberger, et al., 435/252.33, 69.4, 172.1, 172.3, 193, 195, 252.3, 252.31, 252.34, 252.35, 320.1; 930/10, 180; 935/29, 72, 73, 74, 75, 79 [IMAGE AVAILABLE]

US PAT NO: 4,732,859 [IMAGE AVAILABLE] L15: 171 of 191
ABSTRACT:
A novel method for protecting a bacterium from a naturally occurring bacteriophage and the cloning vectors and transformants for carrying out the aforementioned method are disclosed.

172. 4,711,955, Dec. 8, 1987, ▼ Modified ▼ ▼ nuclectides ▼ and methods of preparing and using same; David C. Ward, et al., 536/25.32, 25.6, 26.6 [IMAGE AVAILABLE]

US PAT NO: 4,711,955 [IMAGE AVAILABLE] L15: 172 of 191
ABSTRACT:
Compounds having the structure: ##STR1## wherein B represents a purine, 7-deazapurine, or pyrimidine moiety ▼ covalently ▼ bonded to the C.sup.1' -position of the sugar moiety, provided that when B is purine or 7-deazapurine, it is attached at the N.sup.9 -position of the purine or 7-deazapurine and when B is pyrimidine, it is attached at the N.sup.1 -position;
wherein A represents a moiety consisting of at least three carbon atoms which is capable of forming a detectable complex with a polypeptide when the compound is incorporated into a double-stranded ribonucleic acid, deoxyribonucleic acid duplex, or DNA-RNA hybrid;
wherein the dotted line represents a chemical linkage joining B and A, provided that if B is purine, the linkage is attached to the 8-position of the purine, if B is 7-deazapurine, the linkage is attached to the 7-position of the deazapurine, and if B is pyrimidine, the linkage is attached to the 5-position of the pyrimidine and
wherein each of x, y and z represents ##STR2## either directly, or when incorporated into oligo- and polynucleotides, provide probes which are widely useful.
Applications include detection and localization of polynucleotide sequences in chromosomes, fixed cells, tissue sections, and cell extracts. Specific applications include chromosomal karyotyping, clinical diagnosis of nucleic acid-containing etiological agents, e.g. bacteria, viruses, or fungi, and diagnosis of genetic disorders.

173. 4,711,850, Dec. 8, 1987, Pseudorabies virus mutants, vaccines containing same, methods for the production of same and methods for the use of same; Malon Kit, et al., 435/235.1; 424/205.1, 229.1; 435/172.1, 172.3, 236; 536/23.1 [IMAGE AVAILABLE]

US PAT NO: 4,711,850 [IMAGE AVAILABLE] L15: 173 of 191

ABSTRACT:
The present invention relates to pseudorabies virus mutants containing deletion and/or insertion mutations in a major viral glycoprotein gene, such that no antigenic polypeptides encoded by the viral gene are produced. As a result, animals vaccinated with such do not develop antibodies to the viral glycoprotein and can be distinguished from animals infected with pseudorabies virus field strains and known pseudorabies virus vaccine strains. The present invention also relates to vaccines for pseudorabies disease containing the same, methods for production of the same and methods for use of the same.

174. 4,710,466, Dec. 1, 1987, Method of cloning modified streptomycetes DNA; Charles L. Hershberger, et al., 435/91.41, 91.1, 172.1, 172.3, 252.35, 320.1, 886; 536/23.1, 23.7; 935/31, 35, 36, 37, 59, 73, 75, 79, 80 [IMAGE AVAILABLE]

US PAT NO: 4,710,466 [IMAGE AVAILABLE] L15: 174 of 191
ABSTRACT:
A method of cloning endogenously modified Streptomycetes DNA, which is normally rejected by restrictionless heterospecific hosts, is disclosed. The method uses bacteriophage lambda to construct a genomic library of modified Streptomycetes DNA; such lambda-containing Streptomycetes DNA is replicated to provide a source of non-modified Streptomycetes DNA. This non-modified DNA is subcloned into a selectable cloning vector and used to transform restrictionless hetero-specific hosts. The transformants can then be screened for clones containing genes of interest.

175. 4,707,352, Nov. 17, 1987, Method of radioactively labeling diagnostic and therapeutic agents containing a chelating group; Jannis G. Stavrianopoulos, 424/1.17, 1.45, 1.53, 1.69, 1.73, 179.1; 436/94; 530/300, 350, 402, 403, 405, 406; 536/24.3, 26.6 [IMAGE AVAILABLE]
US PAT NO: 4,707,352 [IMAGE AVAILABLE] L15: 175 of 191
ABSTRACT:

A method of forming a therapeutic or diagnostic agent labeled with a radioactive metal ion, which comprises: contacting an unlabeled therapeutic or diagnostic agent, consisting of a substantially non-metal chelating portion and a chelating portion capable of chelating with the radioactive metal ion, with an ion transfer material having the radioactive metal ion bound thereto and having a binding affinity for the radioactive metal less than the binding affinity of the chelating portion for the radioactive metal ion, wherein prior to contacting the chelating portion is unchelated or is chelated with a second metal having a binding affinity with the chelating portion less than the binding affinity of the radioactive metal ion, whereby a radiolabeled therapeutic or diagnostic agent is formed by the contacting, and separating the radiolabeled therapeutic or diagnostic agent from

the ion transfer material, is disclosed along with various components and kits useful in practicing this method and several variations thereof.

176. 4,705,886, Nov. 10, 1987, Precursor to nucleic acid probe; Corey H. Levenson, et al., 560/159; 562/564; 930/10, 220 [IMAGE AVAILABLE]
US PAT NO: 4,705,886 [IMAGE AVAILABLE] L15: 176 of 191
ABSTRACT:
Nucleic acids may be labeled by intercalating the alkylating intercalation moiety of a labeling reagent into a partially double-stranded nucleic acid to form a complex and activating the complex to cause • covalent • bonding between the reagent and the nucleic acid. Preferably, the labeled nucleic acid is a hybridization probe for detecting nucleic acid sequences capable of hybridizing with a hybridizing region of the nucleic acid. Also preferably the label moiety is non-radioactive. The labeling reagent is of the formula:
[A--[B--L
where A is an alkylating intercalation moiety, B is a divalent organic moiety of the formula: ##STR1## where Y is O, NH or N--CHO, x is a number from 1 to 4, y is a number from 2 to 4, and L is a monovalent label moiety, wherein B is exclusive of any portion of the intercalation and label moieties.
Preferably A is a 4-methylene-substituted psoralen moiety, and most preferably A is a 4'-methylene-substituted-4,5', 8-trimethylpsoralen moiety and L is biotin.

This patent application is a divisional application of copending U.S. Ser. No. 791,332 filed Oct. 25, 1985, now U.S. Pat. No. 4,617,261, which is a continuation-in-part application (CIP) of copending U.S. Ser. No. 683,263 filed Dec. 18, 1984, now U.S. Pat. No. 4,582,789 which is a CIP of copending U.S. Ser. No. 591,811 filed Mar. 21, 1984, now abandoned. This patent application is also related to copending U.S. application Ser. No. 791,333 filed Oct. 25, 1985.

177. 4,670,379, Jun. 2, 1987, Polynucleotide hydridization assays employing catalyzed luminescence; Jeffrey A. Miller, 435/6, 25, 810; 436/501; 536/24.3, 25.32, 25.4; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,670,379 [IMAGE AVAILABLE] L15: 177 of 191
ABSTRACT:
Polynucleotide hydridization assays employing catalyzed luminescence.
178. 4,668,777, May 26, 1987, Phosphoramidite nucleoside compounds; Marvin H. Caruthers, et al., 536/26.5, 26.7, 26.72, 26.8 [IMAGE AVAILABLE]

US PAT NO: 4,668,777 [IMAGE AVAILABLE] L15: 178 of 191

ABSTRACT:
A new class of nucleoside phosphoramidites which are relatively stable to permit isolation thereof and storage at room temperature. The phosphoramidites are derivatives of saturated secondary amines.
179. 4,659,774, Apr. 21, 1987, Support for solid-phase oligonucleotide synthesis; Thomas R. Webb, et al., 525/54.2, 326.1, 326.7, 327.3, 328.2, 328.5, 330.4 [IMAGE AVAILABLE]

US PAT NO: 4,659,774 [IMAGE AVAILABLE] L15: 179 of 191
ABSTRACT:
This invention relates to a support for oligonucleotide synthesis and more particularly to a necleoside-linker/polymer support composite having the general formula

P'--S'
wherein P' is a polymer support which bears oxirane, aziridine or episulfide groups or which contains good leaving groups for nucleophilic displacement; and S' is a nucleoside-linker having the general formula
W--(CH.sub.2).sub.a --X--(CH.sub.2).sub.b --Y--(CH.sub.2).sub.c --Z
wherein W and Z each independently comprise a nucleophile; X and Y which, independently may or may not be present, comprise groups of high hydrophilicity; and a, b, c are integers from 0 to 9, wherein a plus b plus c exceeds 6.

180. 4,652,525, Mar. 24, 1987, Recombinant bacterial plasmids containing the coding sequences of insulin genes; William J. Rutter, et al., 435/252.33, 172.3, 320.1, 849; 930/10 [IMAGE AVAILABLE]

US PAT NO: 4,652,525 [IMAGE AVAILABLE] L15: 180 of 191
ABSTRACT:

A recombinant procaryotic microorganism containing the gene coding for insulin.

181. 4,622,392, Nov. 11, 1986, Thiophospholipid conjugates of antitumor agents; Chung I. Hong, et al., 536/26.22 [IMAGE AVAILABLE]
US PAT NO: 4,622,392 [IMAGE AVAILABLE] L15: 181 of 191
ABSTRACT:
This invention relates to cytotoxic compounds. More particularly, this invention relates to conjugates of antitumor agents, and thiophospholipids exhibiting enhanced antitumor activity to methods for producing such compounds and to pharmaceutical compositions containing cytotoxically effective amounts of such compounds as a primary effective ingredient.

182. 4,617,261, Oct. 14, 1986, Process for labeling nucleic

acids and hybridization probes; Edward L. Sheldon, III, et al., 435/6, 7.24, 7.5, 7.9; 436/94, 501; 536/24.3, 25.32, 25.4, 28.5, 29.54; 548/303.1; 930/220; 935/78 [IMAGE AVAILABLE]

US PAT NO: 4,617,261 [IMAGE AVAILABLE] L15: 182 of 191
ABSTRACT:
Nucleic acids may be labeled by intercalating the alkylating intercalation moiety of a labeling reagent into a partially double-stranded nucleic acid to form a complex and activating the complex to cause • covalent • bonding between the reagent and the nucleic acid. Preferably, the labeled nucleic acid is a hybridization probe for detecting nucleic acid sequences capable of hybridizing with a hybridizing region of the nucleic acid. Also preferably the label moiety is non-radioactive. The labeling reagent is of the formula:
[A--[B--L
where A is an alkylating intercalation moiety, B is a divalent organic moiety of the formula: ##STR1## where Y is O, NH or N--CHO, x is a number from 1 to 4, y is a number from 2 to 4, and L is a monovalent label moiety, wherein B is exclusive of any portion of the intercalation and label moieties.
Preferably A is a 4-methylene-substituted psoralen moiety, and most preferably A is a 4'-methylene-substituted-4,5',8-trimethylpsoralen moeity and L is biotin.

183. 4,587,044, May 6, 1986, Linkage of proteins to nucleic acids; Paul S. Miller, et al., 530/322; 424/179.1; 435/6, 177, 180, 181; 530/358, 391.9; 536/23.1, 25.32, 25.5, 26.12, 26.14, 26.26 [IMAGE AVAILABLE]
US PAT NO: 4,587,044 [IMAGE AVAILABLE] L15: 183 of 191
ABSTRACT:
A nucleic acid-protein conjugate which is specific with respect to a selected living cell is prepared by linking said nucleic acid to a protein specific to said living cell.

184. 4,582,789, Apr. 15, 1986, Process for labeling nucleic acids using psoralen derivatives; Edward L. Sheldon, III, et al., 435/6, 7.5, 7.9; 436/501; 930/10; 935/77, 78 [IMAGE AVAILABLE]

US PAT NO: 4,582,789 [IMAGE AVAILABLE] L15: 184 of 191
ABSTRACT:
A labeling reagent of the formula:

[A][B]L
is prepared where A is an alkylating intercalation moiety, B is a divalent organic spacer arm moiety with a straight chain of at least two carbon atoms, and L is a monovalent label moiety capable of producing a detectable signal, e.g., a signal detectable by spectroscopic, photochemical, chemical, immunochemical or biochemical means. Preferably A is a

4'-methylene-substituted psoralen moiety, and most preferably A is a 4'-methylene-substituted 4,5',8-trimethylpsoralen moiety. This reagent may be used to label nucleic acids, preferably DNA, by intercalating the alkylating intercalation moiety of the reagent into an at least partially double-stranded nucleic acid to form a complex and activating the complex to cause • covalent • bonding between the reagent and the nucleic acid. Preferably, the labeled nucleic acid is a hybridization probe for detecting nucleic acid sequences capable of hybridizing with a hybridizing region of the nucleic acid. Also preferably the label moiety is non-radioactive.
This reagent may also be used in chromosome banding to label specific regions of chromosomes and thereby differentiate them.

185. 4,563,417, Jan. 7, 1986, Nucleic acid hybridization assay employing antibodies to intercalation complexes; James P. Albarella, et al., 435/6, 7.5, 7.9, 966, 975; 436/504; 536/24.3, 25.32; 935/77, 78 [IMAGE AVAILABLE]

US PAT NO: 4,563,417 [IMAGE AVAILABLE] L15: 185 of 191
ABSTRACT:
Nucleic acid hybridization assay methods and reagent systems for detecting a particular polynucleotide sequence in a test medium. An aggregate is formed in the assay reaction mixture comprising intercalation complexes between a nucleic acid intercalator and double stranded nucleic acid associated with the hybridization product of the sequence to be detected and a nucleic acid probe sequence. Hybridization of the probe with the sequence to be detected can then be determined by addition of an antibody, or a fragment thereof, capable of binding with the intercalation complexes in the formed aggregate and measuring the antibody or fragment thereof which becomes bound to such intercalation complexes associated with hybridized probe. In one preferred embodiment, this method eliminates the need to chemically modify the probe in order to form a labeled reagent. In another embodiment, the method provides an advantageous method for labeling the probe by chemical modification.
186. 4,530,904, Jul. 23, 1985, Method for conferring bacteriophage resistance to bacteria; Charles L. Hershberger, et al., 435/172.3, 69.1, 69.3, 69.4, 69.5, 69.51, 69.52, 69.6, 91.41, 252.2, 252.3, 252.31, 252.33, 252.34, 252.35, 320.1, 849; 536/23.2, 24.2; 930/10, 180; 935/29, 72, 73, 83 [IMAGE AVAILABLE]

US PAT NO: 4,530,904 [IMAGE AVAILABLE] L15: 186 of 191
ABSTRACT:
A novel method for protecting a bacterium from a naturally occurring bacteriophage and the cloning vectors and transformants for carrying out the aforementioned method are disclosed.

187. 4,500,707, Feb. 19, 1985, Nucleosides useful in the preparation of polynucleotides; Marvin H. Caruthers, et al., 536/25.34, 26.5, 26.71 [IMAGE AVAILABLE]

US PAT NO: 4,500,707 [IMAGE AVAILABLE] L15: 187 of 191
ABSTRACT:
New and useful intermediate nucleotides bound to an inorganic polymer support, including the preparation thereof, and processes for the conversion to oligonucleotides which are especially useful for the synthesis of polynucleotides, particularly ribonucleic (RNA) and deoxyribonucleic acids (DNA).

188. 4,458,066, Jul. 3, 1984, Process for preparing polynucleotides; Marvin H. Caruthers, et al., 536/25.34, 26.5, 26.71 [IMAGE AVAILABLE]
US PAT NO: 4,458,066 [IMAGE AVAILABLE] L15: 188 of 191
ABSTRACT:
New and useful intermediate nucleotides bound to an inorganic polymer support, including the preparation thereof, and processes for the conversion to oligonucleotides which are especially useful for the synthesis of polynucleotides, particularly ribonucleic (RNA) and deoxyribonucleic acids (DNA).

189. 4,440,859, Apr. 3, 1984, Method for producing recombinant bacterial plasmids containing the coding sequences of higher organisms; William J. Rutter, et al., 435/91.41, 69.1, 69.4, 172.3, 320.1; 935/4, 13, 29 [IMAGE AVAILABLE]

US PAT NO: 4,440,859 [IMAGE AVAILABLE] L15: 189 of 191
ABSTRACT:
Microorganism having a gene derived from a higher organism is produced by isolating cells from a higher organism containing messenger RNA, extracting the messenger RNA, synthesizing a double stranded cDNA using the messenger RNA as a template, inserting the cDNA into a plasmid and transforming a microorganism with the resultant recombinant plasmid.
190. 4,415,732, Nov. 15, 1983, Phosphoramidite compounds and processes; Marvin H. Caruthers, et al., 536/26.5, 26.7, 26.72, 26.8 [IMAGE AVAILABLE]

US PAT NO: 4,415,732 [IMAGE AVAILABLE] L15: 190 of 191
ABSTRACT:

A new class of nucleoside phosphoramidites which are relatively stable to permit isolation thereof and storage at room temperature. The phosphoramidites are derivatives of saturated secondary amines.
191. 4,283,394, Aug. 11, 1981, Cytotoxic nucleoside-corticosteroid phosphodiesters; Charles R. West, et al., 514/26; 536/5, 6, 6.2 [IMAGE AVAILABLE]

US PAT NO: 4,283,394 [IMAGE AVAILABLE] L15: 191 of 191